"Infectious disease is one of the few genuine adventures left in the world. The dragons are all dead and the lance grows rusty in the chimney corner....About the only sporting proposition that remains unimpaired by the relentless domestication of a once free-living human species is the war against those ferocious little fellow creatures, which lurk in the dark corners and stalk us in the bodies of rats, mice and all kinds of domestic animals; which fly and crawl with the insects, and waylay us in our food and drink and even in our love."

This quote is taken from the book **RATS, LICE AND HISTORY** *written in 1935 by the great microbiologist Hans Zinsser, as he reflected on his life in science and medicine and on his efforts to develop the means for preventing typhus and other infectious diseases. Hans Zinsser's thought has challenged several generations of microbiologists and infectious disease specialists, and now it challenges another generation, including the staff of the Center for Infectious Diseases at the Centers for Disease Control. The staff of the Center looks to the demanding challenges of today and tomorrow with the same sense of commitment that guided Hans Zinsser.*

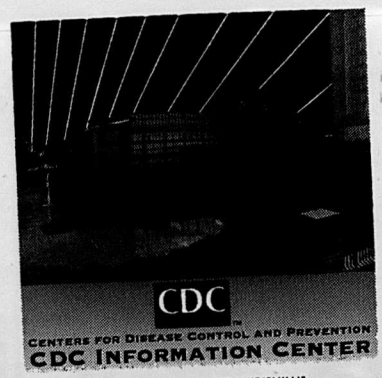
It is hoped that this brochure may entice some readers to take up the same challenge—to inquire further into one of the medical microbiologic/infectious diseases subjects or programs described—to inquire further into career opportunities in these sciences—to inquire further into career opportunities in public service. We would be delighted to respond to any such inquiries.

The Staff of the
Center for Infectious Diseases
Centers for Disease Control

1990

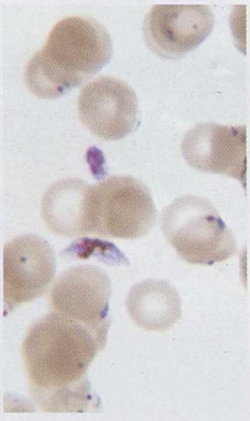
Cover: Scanning electron micrograph, colorized: a human lymphocyte infected with HIV—virions are budding from the cell surface

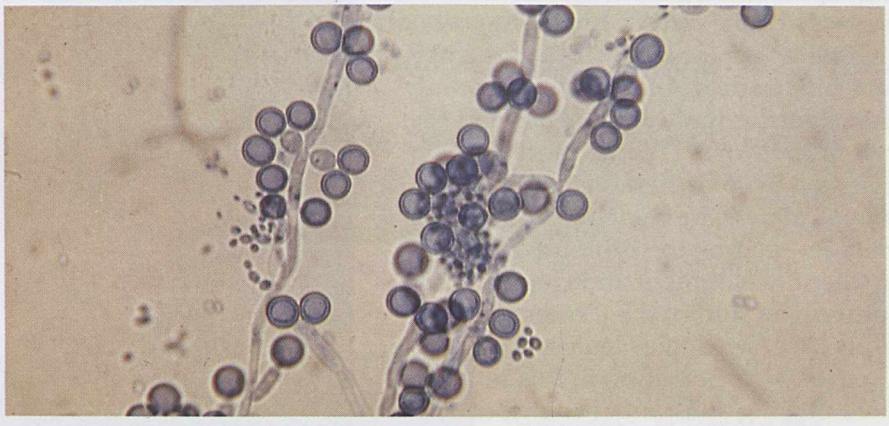
Opposite: top left:—*Plasmodium f*
human red blood cells; top right:-
chlamydospores; bottom left:—*Le*
growth in a nutrient agar tube

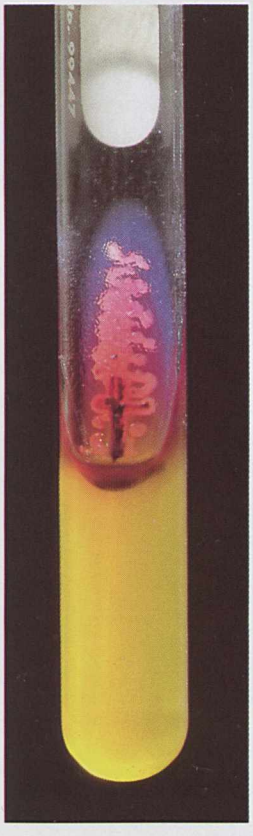


TOWARD THE YEAR 2000

THE CENTER FOR INFECTIOUS DISEASES







Contents

Toward the Year 2000 2

A Century of Discovery—The Scientific Basis for the Prevention and Control of Infectious Diseases 4

Into the 1990s—The Medical Microbiologic/Infectious Disease Sciences of Today 7

Beyond the Year 2000—The Long-term Future of the Microbiologic / Infectious Disease Sciences 9

The Centers for Disease Control 11

The Center for Infectious Diseases 11
- *Mission* 15
- *Facilities* 16
- *Staff* 18
- *A Sampling of Programs, Projects, and Activities* 19
- *World Health Organization Collaborating Centers* 36
- *Divisions and Programs* 37
- *Standing Committees and Interest Groups* 42
- *Organizational Matters* 43
- *For Further Information* 43

THE CENTER FOR INFECTIOUS DISEASES: TOWARD THE YEAR 2000

There is a revolution under way in medical bacteriology, virology, mycology, parasitology, and related clinical sciences that promises great progress in the prevention and control of the important infectious diseases still burdening the people of the United States and the rest of the world. The revolution is represented by an incredible pace of technological development and conceptual change—and by the promise of even greater development and change in the future. The staff of the Center for Infectious Diseases at the Centers for Disease Control is participating in this revolution, making substantial contributions, often in a leadership role, often in a partnership role with colleagues in State and local health departments and other medical, biomedical, and public health institutions.

The history of the sciences at the heart of today's programs for the prevention and control of infectious diseases is brief, spanning only about a century, but it is crowded with wonderful discoveries and practical applications. This history centers on the replacement of centuries-old beliefs, conceptions, and theories by scientific proofs. Scientific proofs established the concept of specificity of infectious disease causation—that is, infectious diseases are caused not by some common miasma (a mysteriously poisonous substance), but rather by specific infectious agents. This concept led to the introduction of specific prevention and control strategies, specific diagnostic tests, and specific therapeutic approaches. This reformation of medical thought involved bitter struggle against entrenched opposition, but in the end the scientific method, the experimental and investigative method, won out.

In a larger sense, the microbiologic/infectious disease sciences have played a paramount role in the reformation of medical thought, overall. The concept of specificity of disease causation and the requirement for verifiable scientific proofs have been extended universally throughout all medical sciences. At the same time, the practical application of the microbiologic/infectious disease sciences has led to improvements in human health and well-being that have exceeded the contribution of any other branch of science.

the microbiologic / infectious disease sciences have played a paramount role in the reformation of medical thought, overall

the concept of specificity of disease causation and the requirement for verifiable scientific proofs, which originated in microbiology, have been extended universally throughout all medical sciences

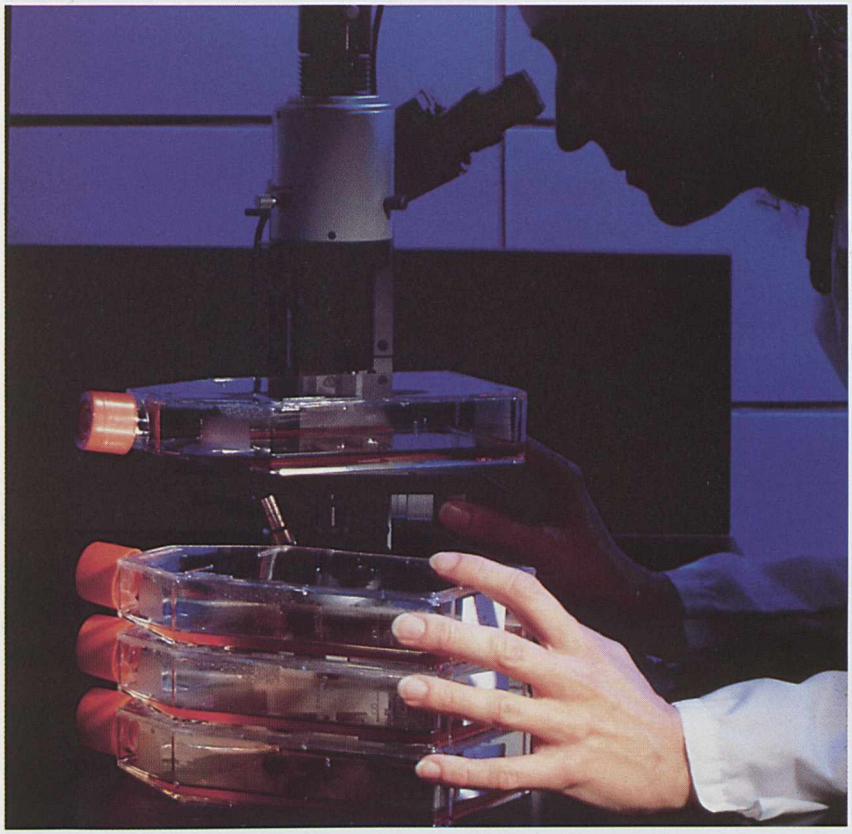
Proof of this practical value of the microbiologic/infectious disease sciences is seen in the effect of scientific breakthroughs on life expectancy worldwide—for example, the great risk of death of mother and baby at childbirth from bacterial sepsis, which was so common in the 19th century, has been eliminated by the application of aseptic gynecologic techniques. Similarly, aseptic techniques have allowed the marvelous achievements of modern surgery.

THE GREAT EPIDEMIC DISEASES		
CONTROLLABLE BY HYGIENE	CONTROLLABLE BY VACCINE	CONTROLLABLE BY CHEMOTHERAPY
PLAGUE	SMALLPOX*	SCARLET FEVER
TYPHUS	MEASLES	MALARIA**
TYPHOID FEVER	INFLUENZA	
CHOLERA	POLIO	
	DIPHTHERIA	
	YELLOW FEVER**	

* ERADICATED WORLDWIDE
** ALSO CONTROLLABLE BY MOSQUITO VECTOR ELIMINATION

For centuries, the "great epidemic diseases" were the most common causes of death everywhere in the world—today, many of these diseases are threats only when vigilance and support for public health programs fail.

In the most striking example of all, one agent of disease, smallpox virus, which at one time was the cause of about 20 percent of all deaths in the world, has been eradicated from the face of the earth. This certainly has been one of the greatest achievements in the history of human civilization.



even as the great epidemic infectious diseases have been conquered, new diseases have emerged, in every case requiring increasing expertise and more complex technological resources than ever imagined

Even as the great epidemic infectious diseases have been conquered, at least in the United States and other developed countries, new diseases have emerged, in every case requiring increasing expertise and more complex technological resources than ever imagined when diseases like smallpox were the target of prevention and control efforts. Today, human immunodeficiency virus (HIV) infection and AIDS may be the best example of the need for advanced expertise, technology, equipment, and facilities—the best example of the need for a revolution in prevention and control strategies. There are many other diseases equally worthy of national attention, each requiring an integration of advanced laboratory and field investigative approaches, each requiring an integration of surveillance, reference diagnosis services, training and consultation, and applied research.

A CENTURY OF DISCOVERY—THE SCIENTIFIC BASIS FOR THE PREVENTION AND CONTROL OF INFECTIOUS DISEASES

Louis Pasteur
1822-1895
the father of the
microbiologic/
infectious disease sciences

The foundation for the microbiologic/infectious disease sciences predates the concept of specificity of infectious disease causation. There are great names and discoveries to be remembered: Hippocrates, the Greek physician and father of medicine, who in the fourth century B.C. made important epidemiologic observations on infectious diseases; Fracastoro, who theorized in 1546 that epidemic diseases were disseminated by minute particles carried over long distances; van Leeuwenhoek, who in 1676 first saw bacteria in his microscope; Hunter, who in 1767 while studying the nature of infection suffered an ill-fated self-inoculation of the syphilis organism; Spallanzani, who in 1775 first grew bacteria in culture; Jenner, who in 1796 introduced vaccination against smallpox; Semmelweis and Holmes, who in the 1840s developed practical methods of cleanliness and disinfection in hospitals; Davaine, who in 1850 first associated an infectious organism, the anthrax bacillus, with disease; and Darwin, Wallace, and Mendel, who from 1859 onward revolutionized thinking in genetics and evolution.

Upon this foundation, Pasteur established the microbiologic/infectious disease sciences, first in 1857 by discovering the specificity of microbial fermentations, then in 1865 by extending this concept to diseases of silkworms, and finally between 1877 and 1895 by extending the concept to animal and human diseases. His early work with pathogenic bacteria centered on septic war wounds; he then turned to anthrax, several other bacterial diseases, and lastly to the viral disease, rabies. In each instance, he moved quickly from studies aimed at discovering the causative agent to the development of specific immunization. In 1885, Pasteur gave the first rabies vaccine to a little boy bitten severely by a rabid dog—that day marks the opening of the modern era of infectious disease research aimed at disease prevention and control. Clearly, Pasteur deserves his title of father of the microbiologic/infectious disease sciences.

Pasteur was followed by Koch, who contributed much to bacteriologic laboratory methods, developing methods for pure culture of bacteria from clinical mixed flora and discovering important bacterial pathogens, such as the causative agents of tuberculosis and cholera. As a result of the work of Pasteur and Koch, isolation and identification of the causative agents of many important bacterial diseases proceeded at breakneck pace around the turn of this century. Another class of microorganisms, the rickettsiae, was added to the list by Ricketts, who in 1909 isolated the causative agent of Rocky Mountain spotted fever.

As this work proceeded, it became possible to consider the natural history and transmission of the bacterial pathogens. Direct transmission by contact with contaminated common objects had been recognized empirically from ancient times—it was substantiated in early laboratory studies of diseases such as childbirth bacterial sepsis, scarlet fever, and diphtheria, and led to concepts of cleanliness, disinfection, isolation, and quarantine. The recognition of contamination of water supplies by the etiologic agents of diseases, such as typhoid fever, cholera, and dysentery, led to the development of sanitary water and sewage systems and to the development of public health regulations and institutions for their enforcement. The recognition of foodborne diseases, such as tuberculosis, salmonellosis, and brucellosis, led to the pasteurization of milk, the sterilization of processed food products, and also

to further development of regulatory systems. Discovery of silent carriers of certain bacterial pathogens as the source of contagion in some food- and waterborne disease episodes further advanced this development.

That some diseases are transmitted sexually was known from antiquity; sexually transmitted diseases were also the subject of the first public health programs aimed at the interruption of transmission. It had also been known from antiquity that some diseases are transmitted from animals to humans (the zoonotic diseases); some of these diseases, for example anthrax, were among the first to be studied in laboratories. Finally, it was recognized that some of the most deadly diseases are caused by agents transmitted to humans from arthropods—plague, transmitted by rat fleas, typhus, transmitted by lice, and many tropical diseases, transmitted by mosquitoes and biting flies. Early laboratory and field work on arthropods and the organisms they transmit led to the application of vector control strategies for disease control.

over the past forty years, outstanding scientists at the Centers for Disease Control have contributed substantially to the march of progress toward the prevention and control of infectious diseases

The foundations of parasitology, immunology, virology, and epidemiology were also established in this same era and became intertwined with the advance of bacteriology and mycology.

In the field of parasitology there are great names and discoveries to be remembered: Bilharz, who in 1851 discovered the parasitic agent of schistosomiasis; Manson, who in 1877 demonstrated the mosquito transmission of filariasis; Laveran, who in 1880 identified malaria parasites in human blood; and Bruce, who in 1894 traced the transmission of trypanosomiasis to the tsetse fly.

In the field of immunology and diagnostics, foundations were established by: Metchnikoff, Bordet, and Ehrlich, who by discoveries made between 1883 and 1909, founded the science of immunology; Loeffler, Roux, Yersin, and Behring, who in 1888 discovered bacterial toxins and antitoxins; Avery and Lancefield, who between 1928 and 1933 developed the basic concepts of infectious disease diagnostics; Porter, Edelman, and Nisonoff, who in 1959 described the structure and function of antibodies; Jerne, who in 1974 conceived the network organization of the immune system; and Kohler and Milstein, who in 1975 developed the first monoclonal antibodies.

In the field of virology great early names and discoveries to be remembered include Beijerinck and Ivanovsky, who in 1898 discovered the first virus; Reed and Carroll, who in 1901 isolated the first human viral pathogen, yellow fever virus; Andrewes, Laidlaw, Smith, and Burnet, who in 1933 first isolated influenza virus, just 15 years after the great influenza pandemic of 1918-19 in which 21 million people died; Blumberg, who in 1963 discovered the "Australia antigen," thereby opening the modern era of viral hepatitis research; and Barre-Sinoussi, Montagnier, and their colleagues, who in 1983 discovered human immunodeficiency virus (HIV), and, along with Gallo and his colleagues, demonstrated it to be the etiologic agent of AIDS.

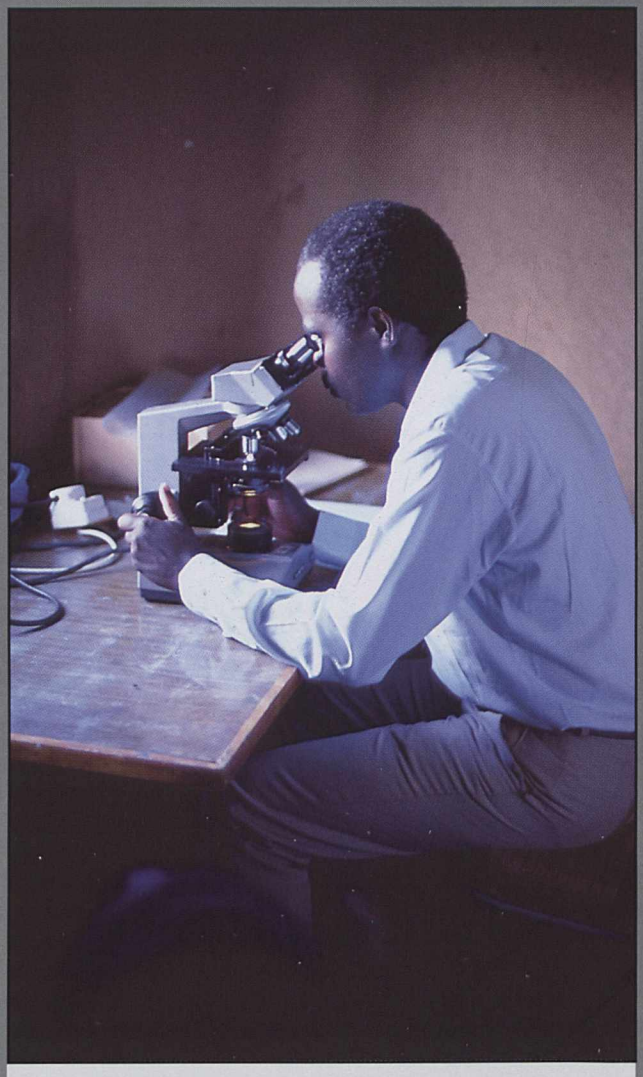
In the field of therapeutics, wonderful discoveries were initiated by Fleming, who in 1929 discovered penicillin; Waksman, who in 1940 discovered streptomycin; Florey, who in 1941 developed the methods for production and clinical application

of penicillin; and Elion and Hitchings, who in 1988 were awarded the Nobel Prize for Physiology in Medicine for pioneering development of a number of important drugs for the treatment of bacterial, viral, and parasitic disease. In the field of vaccinology, a seminal breakthrough was made by Enders, Weller, and Robbins, who in 1949 developed cell culture methods which are now used in most viral vaccine production systems.

In the field of epidemiology, fundamental discoveries were made by Snow, the father of modern epidemiology, who in 1849 developed the methods of modern epidemiology while studying the source of a cholera epidemic at the Broad Street pump in London; Budd, who in 1873 described the epidemiologic features of typhoid fever; Panum, who in the 1870s outlined the epidemiology of measles; and Farr, who in 1885 advanced the use of vital statistics for understanding the epidemiology of infectious diseases.

The opening of the science of molecular biology and its intertwining with the microbiologic/infectious disease sciences calls to mind other great names and discoveries: Avery, Hershey, and Chase, who between 1944 and 1952 used bacteria and bacteriophages to discover that DNA carries all hereditary specificity; Watson, Crick, and Wilkins, who in 1953 discovered the structure of DNA and thereby the molecular basis for hereditary specificity; Nierenberg, Ochoa, Matthaei, Khorana, and others, who between 1961 and 1966 deciphered the genetic code; and Cohen and Boyer, who in 1973 carried out the first experiments in genetic engineering;.

Over the past forty-five years, outstanding scientists at the Centers for Disease Control contributed substantially to the march of progress in infectious disease prevention and control: Langmuir, who in 1951 established the first national epidemiology training program, the Epidemic Intelligence Service, and integrated this into a national field-based investigative epidemiology program; Edwards and Ewing, who in the 1950s and 1960s differentiated many of the pathogenic enteric bacteria; Kissling, who in 1958 developed rabies diagnostic methods and cell culture methods for vaccine production; Shepard, who in 1960 adapted the causative bacillus of leprosy to an experimental animal model, thereby opening antileprosy antibiotic and drug development; Cherry, who in the 1960s developed many fluorescent antibody diagnostic systems for bacterial diseases; Work, Chamberlain, and Sudia, who in the 1960s defined the distribution of the pathogenic arboviruses in the United States; Dowdle and colleagues, who in 1967 distinguished herpes simplex virus strains that cause fever-blisters from those that cause genital disease; and Foege, Hopkins, Nakano, and many others, who during the 1960s and 1970s contributed greatly to field and laboratory aspects of the World Health Organization Smallpox Eradication Program. The accomplishments of these and many other scientists must be seen as revolutionary.



infectious diseases represent paramount health problems in developing countries; among these, none is more important than malaria

INTO THE 1990s: THE MEDICAL MICROBIOLOGIC/ INFECTIOUS DISEASE SCIENCES OF TODAY

The revolution in the medical microbiologic/infectious disease sciences continues today at an ever-increasing pace and scale. We are in the midst of significant change in all aspects of medical bacteriology, virology, mycology, parasitology, and clinical infectious disease sciences.

There is a revolution in epidemiologic investigative approaches. This is evidenced in the sophistication and scale of epidemiologic studies. It was such an epidemiologic investigative program that led to the identification of aspirin use during febrile infections as a risk factor for Reye syndrome; this in turn led to actions that have resulted in a marked decrease in the incidence of the syndrome in the past few years. It was a similar epidemiologic investigative program that unveiled the emerging AIDS epidemic after a cluster of cases of *Pneumocystis carinii* pneumonia was recognized in Los Angeles in 1981. The revolution is also evidenced in the national AIDS/HIV surveillance system, the national salmonellosis surveillance system, the national foodborne disease surveillance system, the national Lyme disease surveillance system, the national hepatitis (sentinel counties) surveillance system, the national/international influenza surveillance system, and many other surveillance systems.

There is a revolution in the computer science underpinning of epidemiologic investigative work. Epidemiologists are increasingly using computer-based surveillance techniques and new sources of data for determining incidence trends of important infectious diseases. Sophisticated computer-based analytic techniques are being used to characterize epidemic and endemic diseases, to identify new disease problems, and to expand knowledge of the impact of long-term sequelae of acute infections. For example, innovative microcomputer-based approaches are being used in the development of hospital-based surveillance of nosocomial infections via the National Nosocomial Infections Surveillance system, and in the analysis of State health department laboratory data on several important infectious disease problems.

epidemiologists and statisticians are increasingly using computer-based surveillance techniques for determining incidence trends of important infectious diseases

There is rapid progress occurring in computer networking in support of national surveillance systems and epidemiologic and laboratory research activities; this includes interconnections between the Centers for Disease Control and State, territorial, and city health departments, and other institutions.

There is a revolution in the statistical science underpinning of infectious disease field and laboratory investigations. The demand for statistical validity to drive public health actions and expenditures involves sound development of protocols and sound data collection, analysis, and interpretation. Statistical models are used to project the future incidence of

disease in populations, using methods ranging from empirical extrapolation of past trends to the construction of mathematical models of future trends.

There is a revolution in the approaches used to discover and identify new etiologic agents. There are still important diseases with no proven causative agent, and there are important new diseases requiring etiologic searching and identification. In these cases, it seems that conventional approaches are dispatched quickly, but when they fail, there is an ever-increasing complexity in the approaches then tried. The determination and insight of the investigator in the field and in the laboratory are still key, but the tools used in the search are today most often products of modern biotechnology. For example, in 1977 the cause of Legionnaires' disease, the bacterium *Legionella pneumophila*, was discovered by integrated field epidemiologic investigation and innovative use of an experimental animal model system. In 1978 the cause of toxic shock syndrome, the bacterium *Staphylococcus aureus*, was recognized by innovative epidemiologic and laboratory investigative approaches. In 1983 the cause of AIDS, HIV, was discovered by insightful clinical and epidemiologic investigative approaches and very sophisticated cell culture systems and molecular biologic assays. Similar integration of field and laboratory approaches led to the discovery in 1987 of a very fastidious new human herpesvirus, the cause of a common childhood disease, roseola infantum. Quite recently the same integrated approach was used in the identification of four genera of microsporidia as important causes of diarrhea and wasting in patients infected with HIV.

the application of recombinant-DNA technology provides a new standard of quality of diagnostic reagents

There is a revolution in diagnostic technology, stemming from monoclonal antibody technology and furthered by innovative equipment design. For example, diagnostic testing instruments are now interfaced with microcomputers to automatically collect and/or digitize information and make it instantly available for tabulation and analysis. Changes in the appearance of diagnostic laboratories are amazing—many now represent a view of the future, but changes in the future will be even more dramatic, and even more supportive of new epidemiologic approaches.

There is a revolution in the practical application of genetic engineering (recombinant-DNA technology), providing us with a new standard of quality of diagnostic antigens and reagents, and new kinds of vaccines and antimicrobial agents. DNA sequencing, molecular modeling, and synthesis procedures employ amazingly sophisticated equipment, as well as powerful computer software and national database networking.

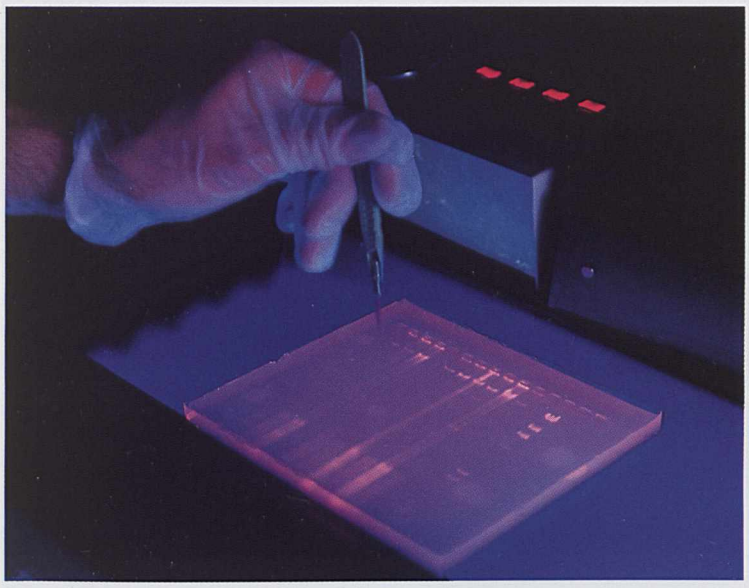
The excitement of medical bacteriology, virology, mycology, parasitology, epidemiology, and clinical infectious disease sciences today is reflected in everything from the awarding of Nobel Prizes, to the growth of national and international microbiologic/infectious disease scientific meetings and congresses, to expanding press and media coverage of infectious disease issues and achievements.

BEYOND THE YEAR 2000: THE LONG-TERM FUTURE OF THE MEDICAL MICROBIOLOGIC / INFECTIOUS DISEASE SCIENCES

Despite a century of progress, the remaining infectious disease problems are awesome—the programs of the Center for Infectious Diseases reflect current priorities for addressing these problems. These programs also reflect the unique approach to disease prevention and control developed by the Centers for Disease Control over the past 45 years. There is a most significant list of new problems which will, in time, be addressed with more and more program resources. New directions for the programs of the Center for Infectious Diseases will reflect the fact that the world's medical microbiologists and infectious disease specialists are just beginning to turn their attention to the role of infectious agents in the many categories of chronic-persistent, degenerative, neurologic, oncogenic, immunopathologic, teratogenic, and other emerging disease issues.

microbiologists are turning their attention to the role of infectious agents in the many categories of chronic, degenerative, and newly emerging diseases

NEUROLOGIC DISEASES: Many bacteria, viruses, fungi, and protozoa infect the brain and spinal cord and cause acute damage; because neural tissues have such poor capacity to repair acute damage, long-term neurologic sequelae are all too common. For example, bacterial meningitis caused by *Haemophilus influenzae* type b, meningococci, and pneumococci often leads to permanent neurologic damage. Viral encephalitis, caused by measles virus, poliovirus, and the arthropod-borne encephalitis viruses, leads to much permanent neurologic impairment in children in developing countries. Yet other infectious agents lead to fatal neurologic disease: HIV dementia, rabies, Creutzfeldt-Jakob disease, subacute sclerosing panencephalitis, progressive multifocal leukoencephalopathy. Finally, there is a growing body of evidence that many neurologic diseases, such as Alzheimer's disease, amyotrophic lateral sclerosis, multiple sclerosis, and transverse myelitis, may be caused by infectious agents, either directly or indirectly via triggering of aberrant cellular changes.



ONCOGENIC DISEASES: Infectious agents cause cancers in humans, either by direct or indirect means. Cancers proven to be caused by viruses, such as those caused by hepatitis B virus (primary hepatocellular carcinoma—the most common cancer in the world), human papillomaviruses (cervical cancer), EB virus (nasopharyngeal cancer, B-cell lymphomas), HTLV-I (adult T-cell lymphoma), and HIV (possibly the trigger of lymphomas), beg the question whether other cancers are also caused by infectious agents. There is a need for additional investigation of other infections wherein the persistent presence of infectious agents in the individual may be the cause of cancers years after the

primary infection. In the future it is clear that more and more cancers of humans will be found to have infectious etiologies or triggering cofactors.

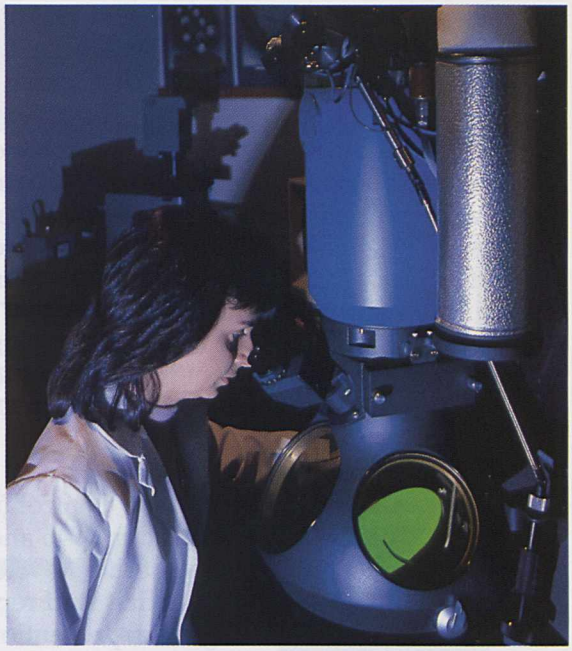
IMMUNOPATHOLOGIC DISEASES (DISEASES CAUSED BY AN ABERRANT IMMUNE RESPONSE): Infectious agents can trigger autoimmune reactivity against the tissues of the infected patient; the classic example is rheumatic heart disease, where antibodies elicited against streptococcal proteins during acute infection then cross-react with normal proteins of heart muscle cells, causing severe damage. The same antibodies can also cause glomerulonephritis. Other autoimmune diseases which may be triggered by infectious processes include Guillain-Barré syndrome, Reiter's syndrome, and psoriasis.

TERATOGENIC DISEASES (DISEASES CAUSING FETAL/NEWBORN DAMAGE OR DYSFUNCTION): Infection of pregnant women can on occasion lead to infection of the fetus or the newborn. Because of the immature state of the immune system of the fetus and newborn, such infections can be severe and the cause of permanent damage. The classic example is the fetal rubella syndrome, which is entirely preventable by prior maternal vaccination. Other infectious agents that may affect the fetus include *Treponema pallidum*, human parvovirus B19, herpes simplex virus, cytomegalovirus, HIV, and toxoplasma.

MAJOR EMERGING AND CHANGING INFECTIOUS DISEASE PROBLEMS: Other emerging and changing infectious disease problems include: (a) infections associated with child care, where the Center for Infectious Diseases has the national leadership role in surveillance, research, and development of prevention guidelines; (b) infectious diarrhea in children, especially fatal diarrhea disproportionately affecting minorities, where the Center for Infectious Diseases has the national leadership role in epidemiologic investigations that will lead to new prevention strategies; (c) influenza and pneumococcal pneumonia, which are important causes of death in older people, where the Center for Infectious Diseases has the national leadership role in surveillance, epidemiologic investigations, laboratory reference diagnosis, and the development of prevention guidelines; (d) infections acquired in hospitals, for example, life-threatening infections acquired in intensive care units, where the Center for Infectious Diseases has the national leadership role in surveillance, epidemiologic investigations, and the development of prevention guidelines; (e) foodborne diseases associated with modern food industries, for example, *Salmonella enteritidis* infections associated with eggs and *Listeria monocytogenes* infections associated with a variety of food products, where the Center for Infectious Diseases has the national leadership role in surveillance and epidemiologic investigations and plays a major role along with other agencies in the development of prevention strategies; (f) hepatitis C infection, newly

despite a century of progress, the remaining infectious disease problems are awesome—the programs of the Center for Infectious Diseases reflect current priorities for addressing these problems

recognized as an important cause of chronic liver disease, where the Center for Infectious Diseases has the national leadership role in surveillance and research that will lead to the development of prevention guidelines; (g) Lyme disease, which is increasing in incidence explosively in many parts of our country, where the Center for Infectious Diseases has the national leadership role in surveillance, epidemiologic investigations, and the development of vector control guidelines, and where a major new research program will lead to national prevention guidelines; (h) diseases caused by very dangerous microorganisms such as Lassa fever virus, where the Center for Infectious Diseases has national responsibility for providing specialized expertise and maximum containment laboratory facilities, as well as overseas field investigative programs; and (i) major tropical diseases, including malaria, dengue, and polio, which represent a devastating burden principally in developing countries, where the Center for Infectious Diseases has national responsibility for providing specialized expertise and laboratory reference diagnostic services, as well as overseas field investigative programs.



the Center for Infectious Diseases provides specialized expertise and laboratory reference diagnostic services for many field investigative programs

THE CENTERS FOR DISEASE CONTROL AND THE CENTER FOR INFECTIOUS DISEASES

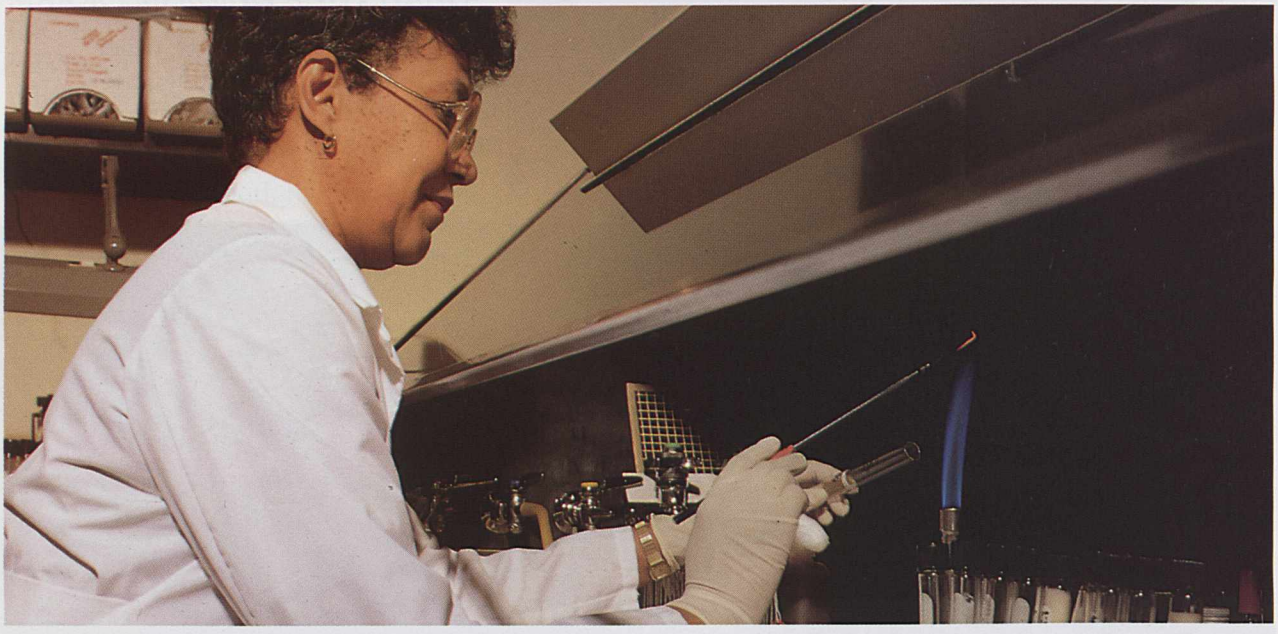
The Centers for Disease Control is the agency of the United States Department of Health and Human Services / Public Health Service responsible for leading national efforts to promote health and prevent disease, disabilities, and premature death. Working with State and local health departments, other Federal agencies, and other organizations and individuals, the staff of the Centers for Disease Control carries out programs aimed at understanding the causes of diseases and developing the means of preventing them.

Major units of the Centers for Disease Control are concerned with chronic diseases, injury, diseases associated with environmental, home, and workplace hazards, and diseases associated with controllable risk factors, such as poor nutrition, smoking, lack of exercise, high blood pressure, stress, and drug misuse. Headquarters of the Centers for Disease Control is in Atlanta, Georgia, but other facilities are located throughout the United States and in several other countries. The Centers for Disease Control has a staff of about 6,000 working in 170 different fields of science and public administration.

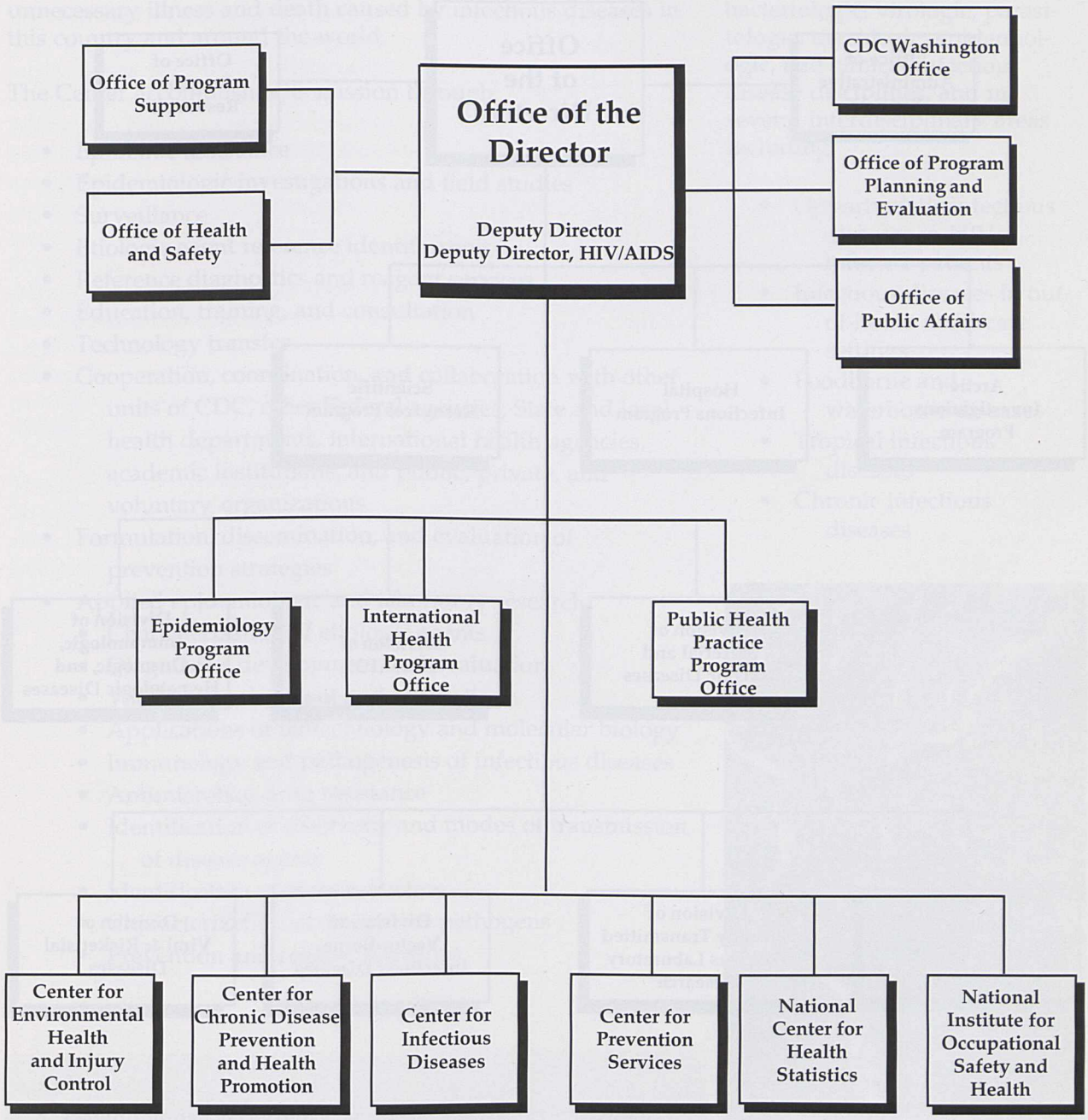
The Centers for Disease Control had its beginnings in the Office of Malaria Control in War Areas. This Office originated in 1946 and was located in Atlanta because of the prevalence of malaria in the Southeast. The first staff represented specialists in the diagnosis, prevention, and control of such diseases as malaria, dengue, schistosomiasis, filariasis, Japanese encephalitis, and other diseases of the Pacific war zone. The original organization soon became the Communicable Disease Center, and in 1967 it became the National Communicable Disease Center. In 1970 the name was changed to the Center for Disease Control and in 1980 to the Centers for Disease Control—many names, but always the same initials. The Centers for Disease Control is now organized into five Centers (the Center for Chronic Disease Prevention and Health Promotion, the Center for Environmental Health and Injury Control, the Center for Prevention Services, the National Center for Health Statistics, and the Center for Infectious Diseases), one Institute (the National Institute for Occupational Safety and Health), and three Program Offices (the Epidemiology Program Office, the International Health Program Office, and the Public Health Practices Program Office).

Today, responsibility for the prevention and control of infectious diseases is focused in the Center for Infectious Diseases and also involves the Center for Prevention Services (particularly in the areas of sexually transmitted diseases, tuberculosis, and vaccine-preventable diseases). The Center for Infectious Diseases was created in 1981 by the merger of components of the former Bureau of Epidemiology and the Bureau of Laboratories.

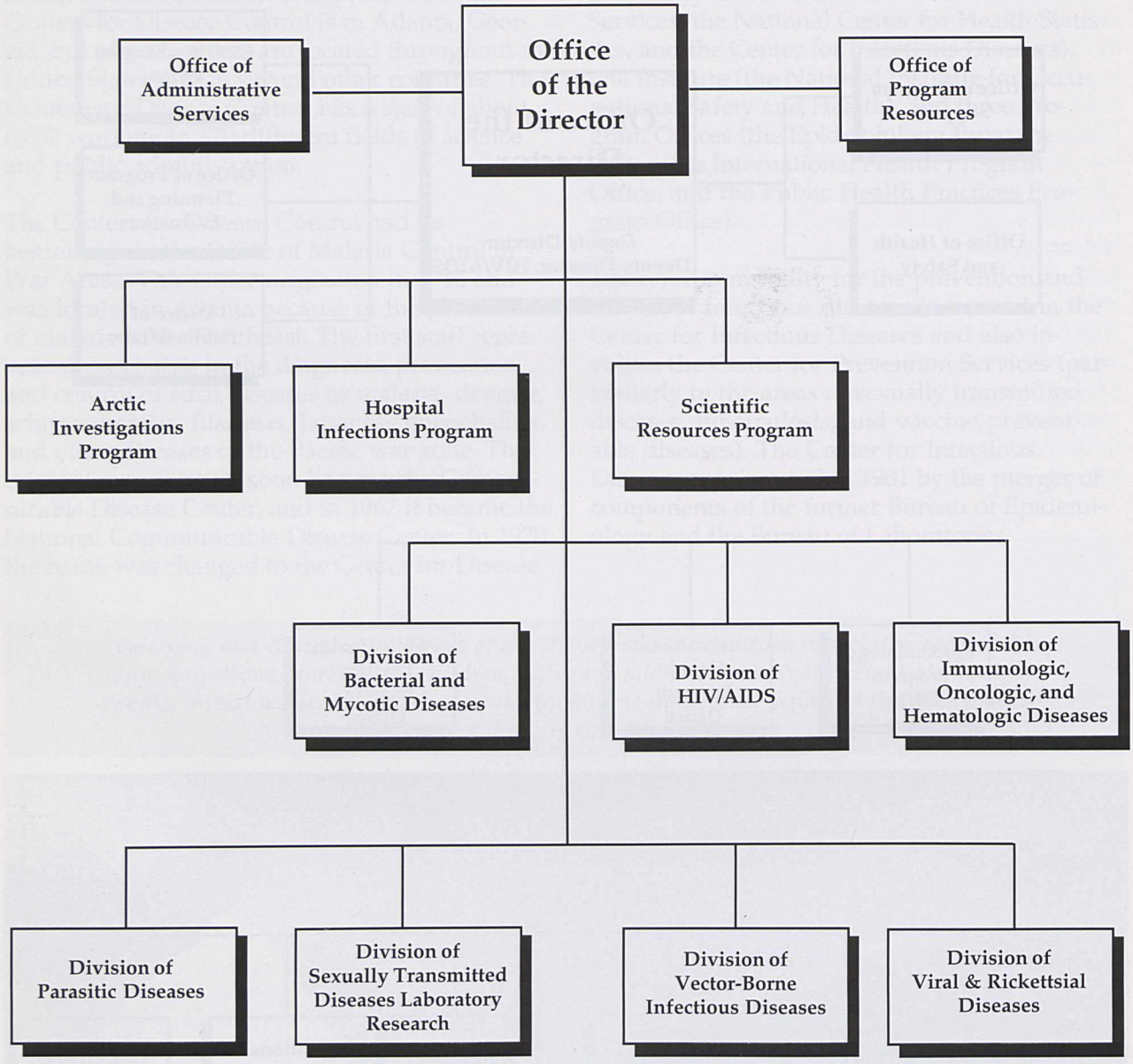
emerging and changing problems of the 1990s include infections associated with child care, infectious diarrheas of children, influenza and pneumococcal pneumonia in older people, infections acquired in hospitals, foodborne infections, hepatitis C, Lyme disease, and others that are equally challenging



THE ORGANIZATIONAL STRUCTURE OF THE CENTERS FOR DISEASE CONTROL



THE ORGANIZATIONAL STRUCTURE OF THE CENTER FOR INFECTIOUS DISEASES



THE MISSION OF THE CENTER FOR INFECTIOUS DISEASES

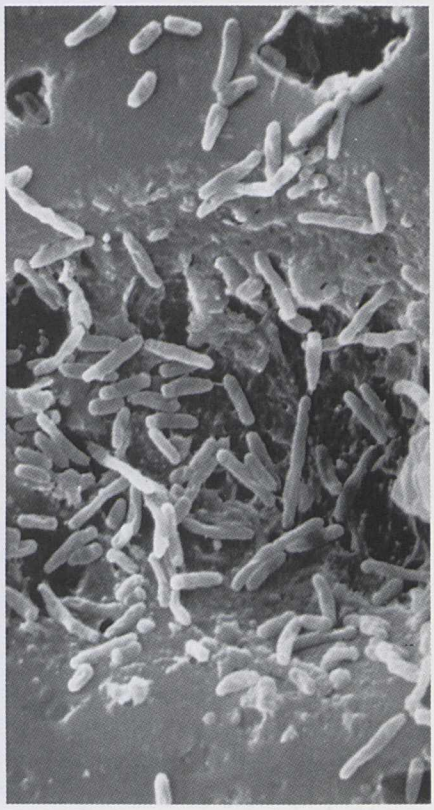
The mission of the Center for Infectious Diseases is to prevent unnecessary illness and death caused by infectious diseases in this country and around the world.

The Center accomplishes its mission through:

- Epidemic assistance
- Epidemiologic investigations and field studies
- Surveillance
- Etiologic agent reference identification
- Reference diagnostics and reagent services
- Education, training, and consultation
- Technology transfer
- Cooperation, coordination, and collaboration with other units of CDC, other Federal agencies, State and local health departments, international health agencies, academic institutions, and public, private, and voluntary organizations
- Formulation, dissemination, and evaluation of prevention strategies
- Applied epidemiologic and laboratory research:
  - Characterization of etiologic agents
  - Diagnostics development and evaluation
  - Vaccine development and evaluation
  - Applications of biotechnology and molecular biology
  - Immunology and pathogenesis of infectious diseases
  - Antimicrobial drug resistance
  - Identification of reservoirs and modes of transmission of disease agents
  - Identification of disease vectors
  - Characterization of dangerous pathogens
  - Prevention and control strategies

The Center operates in all bacteriologic, virologic, parasitologic, mycologic, epidemiologic, and clinical infectious disease disciplines, and in several interdisciplinary areas including:

- Opportunistic infectious diseases in HIV-infected patients
- Infectious diseases in out-of-home child-care settings
- Foodborne and waterborne diseases
- Tropical infectious diseases
- Chronic infectious diseases



Pseudomonas aeruginosa, *scanning electron micrograph, magnification x20,000 —this bacterium is an important cause of bronchopneumonia, septicemia, meningitis, and urinary tract infection, especially in patients with lowered resistance*

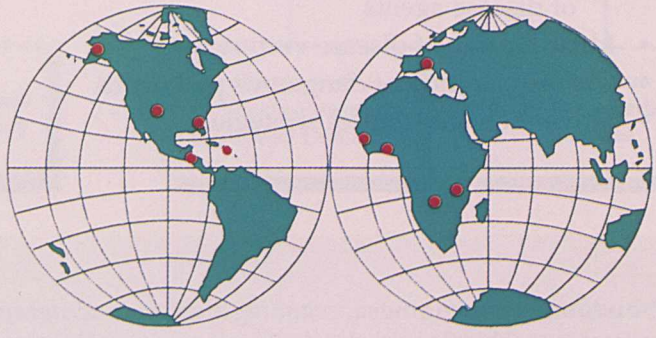
the CDC Viral / Rickettsial Diseases Laboratory, opened in 1988, represents the best of modern biocontainment design and construction

The principal facilities of the Center for Infectious Diseases are located in Atlanta (at Clifton Road, Executive Park, Chamblee, and Lawrenceville). Facilities are also located in Fort Collins, Colorado; Anchorage, Alaska; and San Juan, Puerto Rico. Staff members are also assigned to some State and local health departments in the United States and to public health units in several other countries (Guatemala, Sierra Leone, Cote d'Ivoire, Zaire, Kenya, and the World Health Organization headquarters in Switzerland).

Facilities include offices and associated facilities for computer and data management equipment, general microbiologic laboratories, and highly specialized laboratories that provide for biocontainment and safe use of radioisotopes and toxic chemicals. The Center has developed a Biotechnology Core Facility to support programs with the latest "high tech" equipment and an expert staff. This facility houses equipment and instruments such as oligonucleotide synthesizers, automated nucleic acid sequencers, peptide sequencers, high performance liquid chromatography systems, and specially modified automated thermocyclers for the next generation of development of polymerase chain reaction technology and other microbial gene amplification technologies.

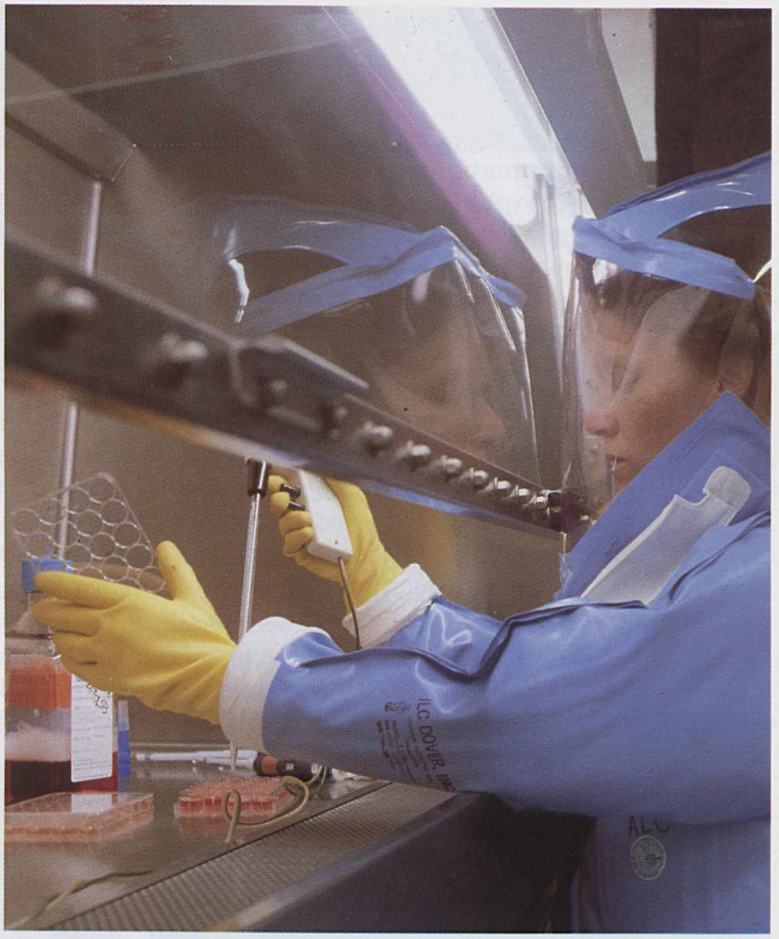
The Center for Infectious Diseases' newest facility is the Viral/Rickettsial Diseases Laboratory, opened in 1988; this facility represents the best of modern biocontainment design and construction. The requirements for a Maximum Containment Laboratory (Biosafety Level 4 laboratory) are so complex and demanding of engineering and laboratory staff expertise that there are only two facilities in the United States, one at the Centers for Disease Control

Center for Infectious Diseases
Locations

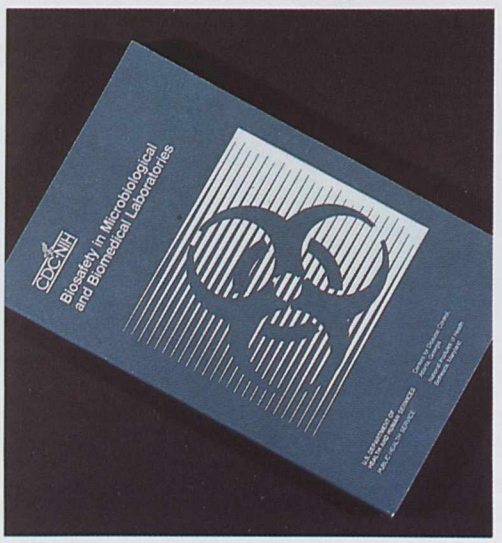


and the other at Fort Detrick (U.S. Army), and only a few others elsewhere in the world. The staff member wears a full-body pressurized "space suit" connected by hose to a breathing air system. Entry into and exit from the laboratory are through an air-lock system, the exit after a chemical shower in a chamber where the exterior of the "space suit" is thoroughly decontaminated. Within the laboratory, work with infectious organisms is carried out using all the same kinds of biocontainment equipment, such as biosafety cabinets, and all the same kinds of safe practices and procedures as are used in other laboratories. All in all, this laboratory represents the ultimate in laboratory facilities and operations design for the protection of the laboratory staff and the environment from pathogens.

The facilities of the Center for Infectious Diseases are operated in accord with national biosafety standards for microbiologic and biomedical laboratory operations. These standards are set under the auspices of the Centers for Disease Control and the National Institutes of Health. Work with organisms not known to cause disease is done at Biosafety Level 1 (BSL 1), and work with organisms that represent only a modest risk, such as viruses that cause the common cold and bacteria that cause diarrhea, is done at BSL 2. Work with organisms that can cause serious disease, but for which vaccines or antibiotics are available, such as the tuberculosis bacillus, rabies virus, and the rickettsia that causes Rocky Mountain spotted fever, is done at BSL 3. Work with organisms that pose a high risk of life-threatening disease and for which no vaccines or antibiotics are available, such as the viruses that cause hemorrhagic fever and encephalitis, is done at BSL 4 (the Maximum Containment Laboratory).



at Biosafety Level 4 the staff member wears a full-body pressurized "space suit" connected by hose to a breathing air system—exit from the laboratory is through an air-lock system and a chemical shower

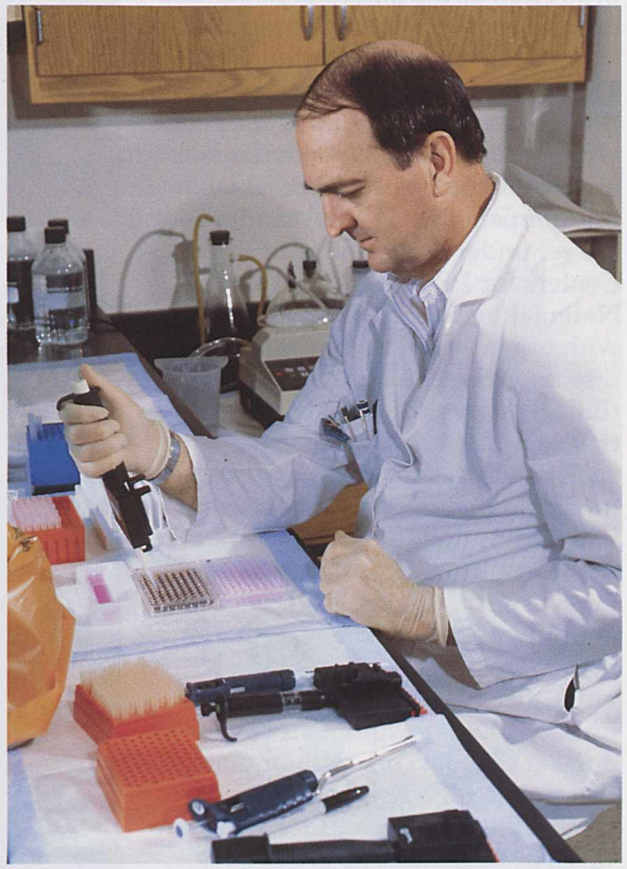


the facilities of the Center for Infectious Diseases are operated in accord with national biosafety standards for microbiological and biomedical laboratory operations

THE STAFF OF THE CENTER FOR INFECTIOUS DISEASES

The key to programmatic and institutional development within the Center for Infectious Diseases is its staff—the Center for Infectious Diseases has a remarkable staff, dedicated and nationally and internationally renowned. Evidences of distinction of the professional staff include receipt of many national and international awards, leadership in many professional societies, publication of many significant papers, and election to many editorial and professional boards and committees. Many members of the professional staff are involved in education and training, most notably in advanced technical training and disease investigation training (especially in concert with the World Health Organization and other international agencies). Many staff members are also involved in formal teaching through university affiliations. It is clear that as the generations follow one another, the staff of the Center for Infectious Diseases keeps getting better and better. The newest members of the staff are outstanding—although these staff members could have chosen other employment opportunities, they have chosen the Center for Infectious Diseases and the Centers for Disease Control because of the unique opportunity offered to combine scientific and public service activities for the betterment of the health of the people of the United States and the rest of the world.

the staff of the Center for Infectious Diseases integrates the many fields of the medical microbiologic / infectious diseases sciences

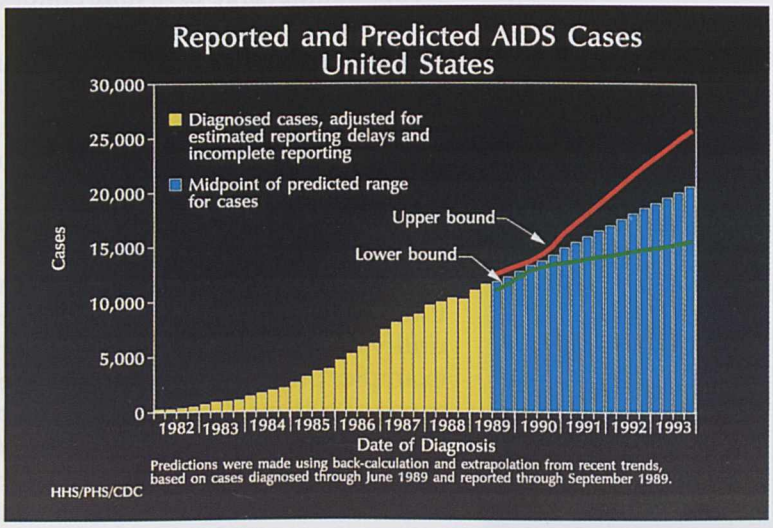


the integration of epidemiologic, laboratory, and statistical sciences allows comprehensive assessment of complex disease problems

A SAMPLING OF PROGRAMS, PROJECTS, AND ACTIVITIES OF THE CENTER FOR INFECTIOUS DISEASES

The following are but some examples of the programs, projects, and activities being carried out in the Center for Infectious Diseases at this time. These examples have been chosen to reflect the breadth of the overall program of research and service, and the programmatic depth, technologic complexity, and demand for staff expertise and energy that are called for in efforts to solve today's infectious disease problems.

HUMAN IMMUNODEFICIENCY VIRUS INFECTIONS AND AIDS: HIV infection and AIDS are the most important infectious disease problems in the United States today. By the end of 1989, more than 100,000 cases of AIDS had been reported, more than 30,000 cases in 1989 alone. These numbers will continue to increase in the next few years as many of the one million persons who are infected in the United States develop AIDS. The goal of the HIV/AIDS program is to define and test means for the prevention and control of virus transmission: this involves definition of the epidemiology and natural history of HIV infection and identification of population groups at risk. This is accomplished through AIDS case surveillance, HIV serosurveillance, and domestic and international epidemiologic and laboratory investigations. The national HIV seroprevalence survey system involves over 30 metropolitan areas and selected populations including military recruits, blood donors, clinic patients, intravenous drug users, childbearing women, Job Corps applicants, prisoners, and college students. Sentinel hospital-based surveillance is also being used to determine trends. Epidemiologic studies are focused on homosexual men, IV drug users, persons with hemophilia, persons with transfusion-associated disease, female prostitutes, sex partners of persons with AIDS or at increased risk for AIDS, babies born of infected mothers, health-care workers, and long-term survivors. International collaboration involves studies in Zaire, Cote d'Ivoire, and Thailand and includes epidemiologic and laboratory studies on HIV-1 and HIV-2.



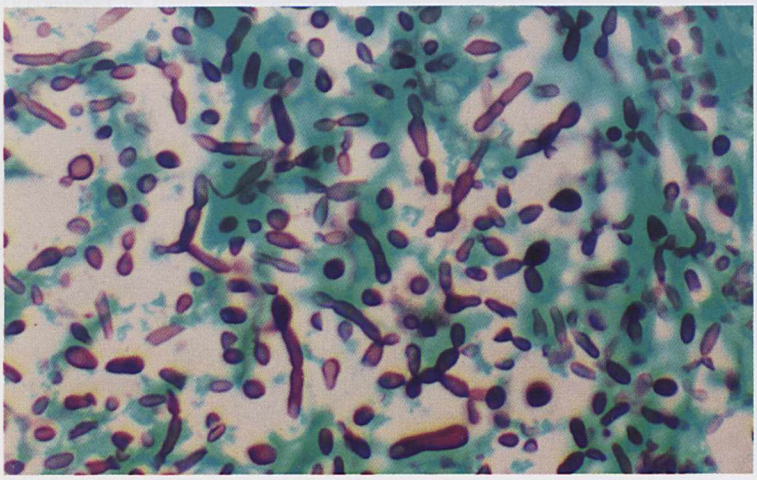
the dynamics of the AIDS epidemic in the United States to date, and the projected number of cases in the future

OPPORTUNISTIC INFECTIONS IN HIV-INFECTED PATIENTS: Patients with AIDS develop certain opportunistic infections, such as *Pneumocystis carinii* pneumonia, *Mycobacterium avium-intracellulare* disease, and invasive candidiasis, that in the past were seen only in patients whose immunity was compromised by malignancies or medications. However, it has also become apparent that other infections that have not traditionally been considered opportunistic, such as pneumococcal disease and systemic salmonellosis and shigellosis, are occurring in HIV-infected patients, often at rates 100-fold greater than expected. These infections often occur before manifestations of profound immunodeficiency; an example of this is pneumococcal bacteremia, which has been seen commonly in HIV-infected persons in San Francisco. Until prevention or control of HIV infection is possible, strategies for control and prevention of these opportunistic infections must be improved and implemented.

An interdisciplinary program is in place in the Center for Infectious Diseases with the aim of doing this. Epidemiologic studies of specific infections are being conducted to determine rates of disease in different populations infected with HIV. Laboratory studies are being conducted to improve diagnostics. Such studies will lead to recommendations for better preventive and treatment regimens. As an example, studies of populations at risk for HIV infection (e.g., young men in certain geographic areas) have shown increased risk for shigella bacteremia; this information is being used to guide early diagnosis, long-term prophylactic antibiotic therapy, and targeted preventive educational programs.

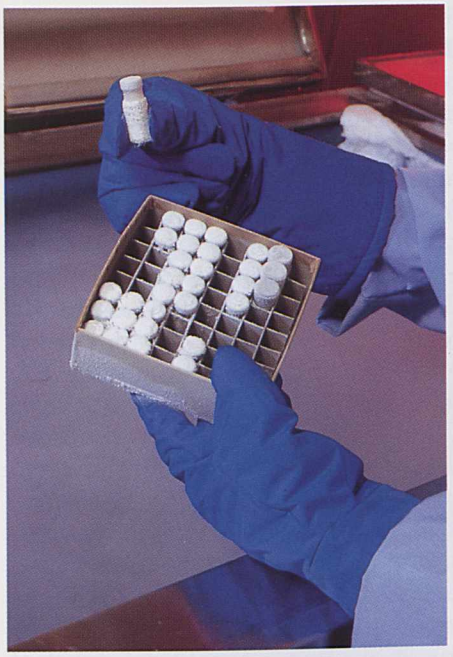
INFECTIONS IN HOSPITAL INTENSIVE CARE UNITS: In the United States, hospital-acquired infections affect two million patients annually; direct extra patient care costs are approximately $3.5 billion. Infections in immunocompromised patients and in patients in intensive care units account for a large proportion of all infections. Programs of the Center for Infectious Diseases to reduce infection rates in intensive care units include the development of surveillance systems, the assessment of infection trends and rates, the identification of risk factors for infection, and the development of preventive intervention strategies. The National Nosocomial Infections Surveillance system is operated to provide data and to guide recommendations for intervention; through this program, patterns of infection can be detected at national, hospital, hospital unit (e.g., intensive care unit), procedure (e.g., intravascular catheter usage, coronary artery bypass surgery), ward, or patient level. Using these data, guidelines for the prevention of specific infections (e.g., pneumonia, urinary infections) are being developed and implemented.

patients with AIDS develop debilitating opportunistic infections, such as pneumonia caused by **Cryptococcus neoformans,** *as shown in this stained section of human lung obtained at autopsy*



gene amplification technology (the polymerase chain reaction—PCR) allows the detection of very small amounts of DNA or RNA of infectious agents—it has made possible the detection of HIV infection early in the course of infection

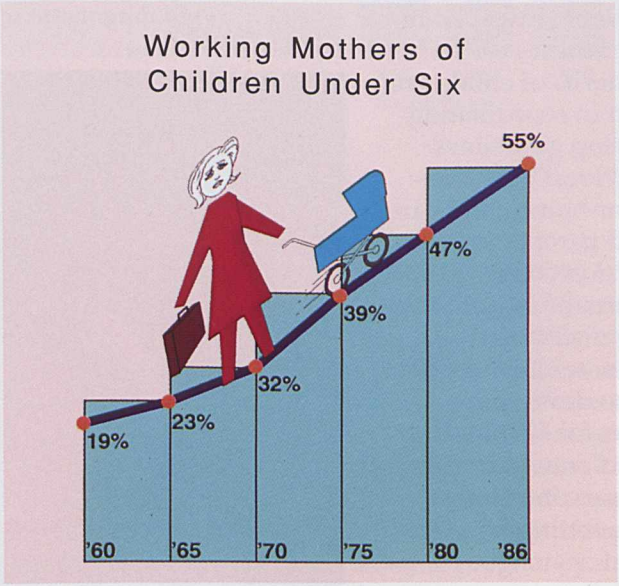
Neonatal intensive care unit patients have one of the highest rates of hospital-acquired infection of any hospital population. It is estimated that approximately 9,000 infant deaths are caused by hospital-acquired infections annually. Studies are under way to evaluate infection risk for particular invasive procedures used in neonatal intensive care units; studies are also focused on the utility of rapid diagnostic tests. For example, invasive candidiasis is the cause of serious illness and mortality in immunocompromised newborn patients. Epidemiologic and laboratory studies are determining the utility of a rapid diagnostic test that allows early diagnosis for guiding therapy.



there are 28 WHO Collaborating Centers for Reference and Research in the Center for Infectious Diseases

SURGICAL WOUND INFECTIONS: Surgical wound infections account for approximately 30 percent of all hospital-acquired infections; these infections lead to prolonged hospitalizations, increased hospital costs, and increased mortality. Many surgical wound infections can be prevented via the establishment in hospitals of an active infection surveillance and control program. For example, a surgical patient infection risk index and a procedure-specific infection rate index can be used as parts of a system for evaluating the infection rate obtained by each surgeon. This kind of system, established via recommendations and training from the Center for Infectious Diseases, via its National Nosocomial Infections Surveillance system, has been shown to substantially reduce the rate of surgical wound infections.

INFECTIOUS DISEASES IN OUT-OF-HOME CHILD CARE: In recent years, shifts in the structure of the American family have resulted in dramatic changes in the care and rearing of young children. The proportion of children in out-of-home child care has increased substantially; currently, an estimated 11.6 million children spend a minimum of ten hours per week in out-of-home child care. The fastest growing subgroup of working mothers are those with children under one year of age, with fully half of these women employed. This trend is likely to continue; by the year 2000 it is estimated that more than 75 percent of mothers with children under six years of age will be working outside the home. The economic impact of child-care-associated morbidity is great: working mothers are forced to miss one to four weeks per year to care for their sick children. Studies suggest that over 60 percent of employee absenteeism may be due to unmet child-care needs, particularly those of sick children. Infectious diseases are the most important causes of morbidity in child-care centers, with respiratory and diarrheal illnesses being most common. Depending on the disease, children attending out-of-home child care are estimated to have a 2- to 18-fold increased risk of becoming ill compared with children not attending a child-care center. The most common diarrheal pathogens in children in out-of-home child care are *Giardia lamblia, Shigella* species, and rotavirus—agents spread by person-to-person contact. The vast majority of respiratory infections in child-care centers are viral in nature, but otitis media and its sequelae are also common. Some infectious agents appear to be endemic in the child-care center setting: *Giardia lamblia* can become endemic, causing repeated cases of diarrhea. About 12–15 percent of all reported cases of hepatitis A have been associated with child-care centers; the spread of hepatitis from children in child-care centers to family members and then to the community has become an important problem. Nearly all states have regulations



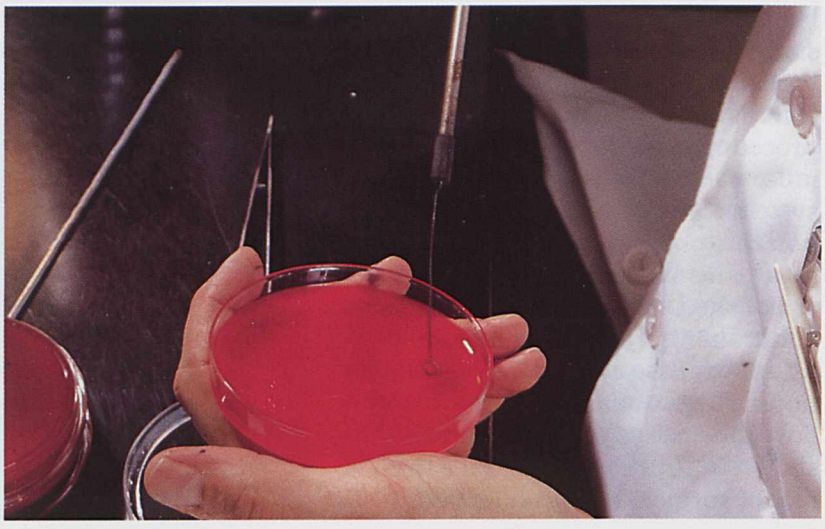
shifts in the structure of the American family have resulted in great increases in out-of-home child-care — this has led to increases in certain childhood infectious diseases

the Center for Infectious Diseases, together with professional organizations, State and local health authorities, child-care providers, and parents' groups, is developing disease prevention guidelines for child-care centers

for the control of infectious diseases in licensed child-care centers; however, scientific data to support recommendations are lacking. Risk factors are not well understood; for example, the management of ill children in child-care centers and the exclusion of sick children are subjects of great controversy. Despite the importance of out-of-home child-care health issues to State and local health departments, resources are limited; many agencies need guidance in developing systems for prevention of infectious and vaccine-preventable diseases (injuries and environmental hazards are also problems). The Center for Infectious Diseases is actively involved in epidemiologic studies to determine patterns of child-care utilization and in coordinating efforts to develop guidelines with State and local health authorities, out-of-home child-care providers, and parents' groups. National infection control guidelines, in the form of information kits, are being distributed widely. The Center for Infectious Diseases is also developing diagnostic tests for *Giardia* and respiratory and enteric viruses to facilitate disease control programs in these settings.

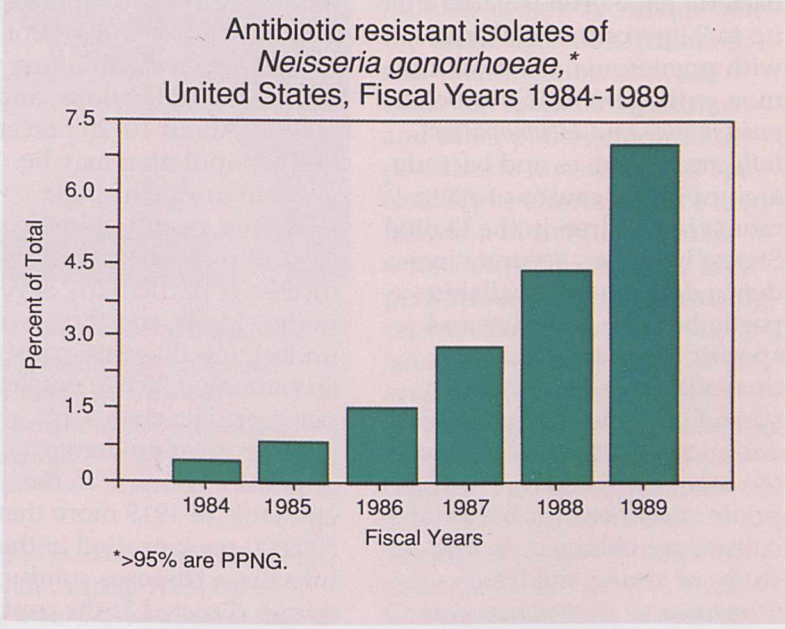
FOODBORNE AND WATERBORNE DISEASES: Recent public concern over foodborne disease is justified; there is evidence that disease incidence is increasing. Estimates of disease incidence range from a few million to 80 million cases per year; comprehensive data are lacking, but it seems clear that the higher estimates are closest to reality. Foodborne disease results in over 9,000 deaths and more than $1 billion in economic losses each year. Changes in animal husbandry practices, food processing, and the development of more ready-to-eat food products have created new situations where pathogens are introduced into foods. Changes in food distribution systems involving fewer but larger processors are increasing the number of large, interstate outbreaks of disease. The Center for Infectious Diseases has identified a series of important emerging problems: grade A shell eggs harboring *Salmonella enteritidis* are causing epidemic foodborne disease in the northeastern United States, and the problem is spreading to other parts of the country;

the Center for Infectious Diseases, in cooperation with other agencies, is working to better identify important causes of foodborne disease and to develop rapid diagnostic tests for foodborne pathogens



processed foods contaminated with *Listeria monocytogenes* are causing over 1,600 illnesses and 400 deaths each year in pregnant women, their fetuses and newborn babies, the elderly, and persons with underlying diseases (recalls of products containing *Listeria* have cost millions of dollars in recent years); ground beef, contaminated with a newly recognized pathogenic strain of *Escherichia coli*, serotype O157:H7, is causing many outbreaks and sporadic cases of hemorrhagic diarrhea and hemolytic uremic syndrome (the most common cause of acute renal failure in children); and raw or undercooked shellfish are responsible for hepatitis, cholera, and *Vibrio vulnificus* infections (the latter, although rare, can have a 50 percent mortality rate). There are other disturbing trends: *Salmonella and Campylobacter* infections are increasing steadily, nearly always in association with consumption of foods of animal origin. In 1985, a single dairy caused 200,000 cases of salmonellosis. Currently available data are too limited to lead to fully effective prevention and control programs. Specific foods that cause large numbers of illnesses can escape recognition, and critical control measures are not identified. To deal with these foodborne disease problems, the Center for Infectious Diseases, in cooperation with other Federal agencies, is instituting a program that will better identify important causes of foodborne disease, determining which foods are causing disease, developing rapid and accurate diagnostic tests for foodborne pathogens, and determining strategies for the prevention of foodborne disease. This program will guide critical-control-point food inspection activities of regulatory agencies and will lead to more rapid public health response to outbreaks of foodborne disease.

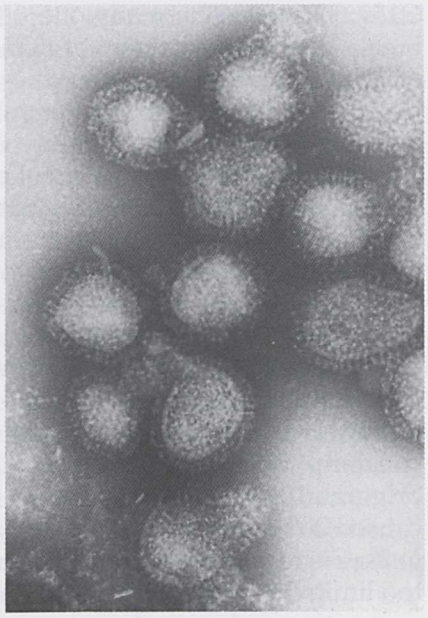
GONORRHEA: Although the incidence of gonorrhea has been decreasing steadily since 1978, it is still the most common of the reportable infectious diseases in the United States (in 1988, 688,000 cases were reported to the Centers for Disease Control). Pelvic inflammatory disease and disseminated gonococcal infections may occur if uncomplicated infections are not treated. Pelvic inflammatory disease is the most important complication; it occurs in approximately 8 percent of women with gonorrhea, resulting in tubal damage and an increased probability of subsequent ectopic pregnancy. It has been estimated that the direct cost of gonococcal pelvic inflammatory disease is $1.7 billion per year. The challenge of controlling gonorrhea remains formidable because of an increase in the proportion of *Neisseria gonorrhoeae* isolates resistant to currently used antimicrobial drugs. Penicillin- and tetracycline-resistant gonococcus strains have increased dramatically in the past few years, exceeding 20 percent of isolates in many areas. Studies are under way in the Center for Infectious Diseases to further define the magnitude and nature of this antimicrobial drug resistance and to develop guidelines for proper antimicrobial drug usage.



SEXUALLY TRANSMITTED CHLAMYDIAL INFECTION: Chlamydial infection is not reportable, but there is good evidence that it is the most common sexually transmitted infection in the United States, exceeding the combined number of gonorrhea and syphilis infections. Three to five million cases of acute infection occur annually, leading to about 500,000 cases of pelvic inflammatory disease. The cost of treating chlamydial pelvic inflammatory disease exceeds $2 billion annually. Sequelae following pelvic inflammatory disease include infertility and ectopic pregnancy. Infants born of

infected mothers are exposed at birth and are at risk for chlamydial conjunctival infection and pneumonitis. Lack of awareness of the disease by both public and private sector health-care providers, together with the paucity of laboratories providing diagnostic testing, have hampered disease control efforts. Research on genital chlamydia infections in the Center for Infectious Diseases includes collaborative efforts to identify populations at risk and to improve diagnosis.

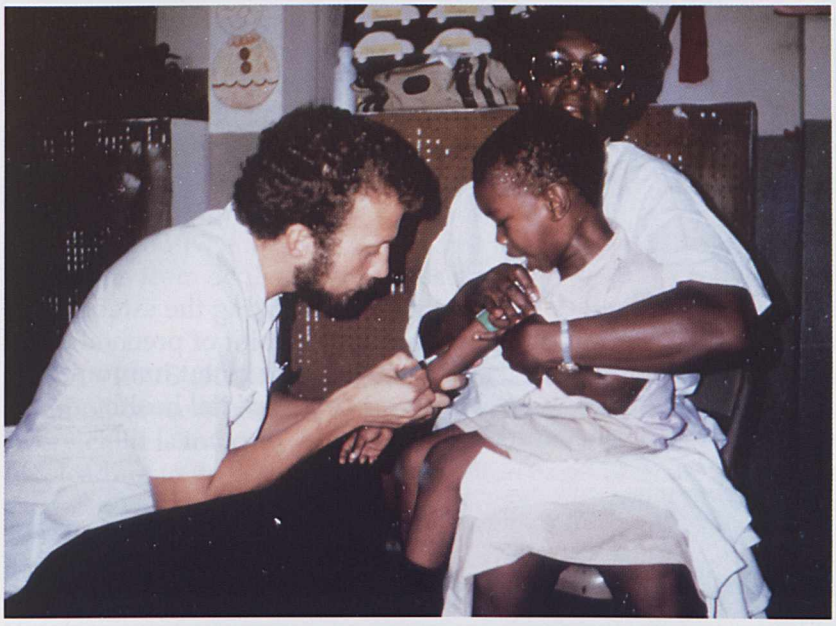
PEDIATRIC RESPIRATORY DISEASE: Acute lower respiratory infection is the leading cause of death in children in the world. In developing countries, bacteria have been isolated from up to 92 percent of children with pneumonia; the most common pathogens are *Streptococcus pneumoniae* and *Haemophilus influenzae*. Viruses and bacteria are important causes of pneumonia in children in the United States; however, accurate incidence data are not available, partly because sensitive and specific diagnostic tests are unavailable or not in widespread use, and partly because antimicrobial drug treatment is too often started before appropriate specimens for bacterial culture are obtained. In one study of young children, *Streptococcus pneumoniae* was isolated from half of culture-confirmed bacterial pneumonias and *Haemophilus influenzae* type b from another third. The best estimate of the incidence of pneumococcal bacteremia in children under 2 years of age in the United States is 1.5 cases per 1,000 children per year. Pneumococcal bacteremia may be associated with pneumonia, especially in very young children, and with otitis media. Improved methods for rapid diagnosis of pneumococcal disease, involving immunologic probes and other molecular biologic techniques, are under development in the Center for Infectious Diseases. These methods are being integrated into prevention programs being developed in collaboration with others, nationally and internationally. For example, a large pneumococcal vaccine trial in infants (testing a protein-polysaccharide conjugate pneumococcal vaccine) is in preparation in The Gambia, where the incidence of pneumonia is very high; this trial will yield information on the epidemiology and etiology of lower respiratory infections, as well as on the efficacy of the vaccine, which will be immediately extendable to the United States and the rest of the world.



a never-ending watch is kept on the changing genetic properties of influenza virus

INFLUENZA: Influenza remains the last great epidemic disease—it returns every winter to afflict people of all ages and from all walks of life. Influenza epidemics are responsible for spreading waves of work and school absences, physician office visits, hospitalizations, and deaths. About 10–20 percent of the population may become ill during a single epidemic, resulting in direct costs of over $10 billion. The disease is particularly severe in the elderly and those with underlying diseases, causing an estimated 50,000 deaths per year. The chance of another great epidemic remains a concern: in the epidemic of 1918 more than 500,000 persons died in the United States alone. The Center for Infectious Diseases conducts epidemiologic and laboratory activities directed at the control and prevention of influenza. A never-ending watch is kept on the occurrence of influenza worldwide and on the changing properties of virus isolates. Characterization of virus strains leads to the identification of new variants. Discovery of new variants, in turn, begins a chain of actions that ends with reformulation of vaccines. Each year there is a race against time to have the best vaccine available before a new variant arrives in the United States. During epidemic periods, the Center for Infectious Diseases conducts surveillance to assist health-care providers in making decisions concerning vaccine and antiviral drug use. Laboratory research is aimed at improving vaccines, monitoring antiviral drug resistance, and developing rapid diagnostic tests.

PNEUMOCOCCAL PNEUMONIA IN THE ELDERLY: Pneumococcal pneumonia accounts for an estimated 150,000 to 500,000 cases and 50,000 deaths in the United States each year. Individuals with underlying diseases are more susceptible to serious illness and death; over 40 percent of elderly persons with bacteremia may die of this illness, and patients with AIDS have a risk of bacteremia and death 100-fold greater than would be the case otherwise. Antimicrobial drugs have significantly decreased the mortality of pneumococcal pneumonia, yet the increasing incidence of penicillin and multiple-drug-resistant strains of pneumococci are an important concern. Through hospital-based



the Center for Infectious Diseases is assessing the impact of vaccination against pneumococcal pneumonia—vaccine-based prevention strategies are being developed in collaboration with State and local health departments and academic institutions

studies, the Center for Infectious Diseases is examining the emergence of antibiotic resistance, and is collaborating with other agencies and institutions in developing alternative approaches to therapy. Pneumococcal vaccines are available in the United States but are underutilized. The Center for Infectious Diseases is conducting a variety of epidemiologic and laboratory studies to measure the impact of vaccination on each serotype of pneumococci responsible for substantial disease. Vaccine-based prevention strategies are being developed in collaboration with colleagues in State and local health departments and academia; the goal is to prevent disease, especially in high-risk populations. Parallel laboratory research activities, involving novel molecular biologic techniques, are aimed at developing rapid diagnostic tests for pneumococcal disease, so as to better guide vaccine usage and antibiotic therapy.

TUBERCULOSIS: Tuberculosis is often thought of as a global health problem centered in developing countries, but there are over 20,000 cases and 1,000 deaths each year in the United States. In 1989, tuberculosis was targeted for elimination from the United States, but an increase in the number of cases in HIV-infected persons, particularly IV drug users, has confounded that goal, and now the target date for elimination has been moved to the year 2010. Control and elimination of tuberculosis will depend upon the development and use of better diagnostic techniques and better therapeutic regimens. The Center for Infectious Diseases is investigating a number of new techniques for the rapid detection, isolation, and identification of *Mycobacterium tuberculosis* strains and other pathogenic and opportunistic mycobacterial species. These efforts involve identification of unique mycolic acids in mycobacteria by high performance liquid chromatography, determination of mycobacterial species specific fatty acid profiles by gas-liquid chromatography, identification of specific mycobacterial proteins by immunologic methods, and assay of DNA sequences unique to each mycobacterial species and strain. The latter will lead to systems for the detection and identification of small numbers of mycobacteria via amplification of their DNA (using the polymerase chain reaction—PCR). These approaches will lead to earlier detection of infected persons—a crucial element in interrupting the chain of transmission and eliminating the burden of this devastating disease.

HEPATITIS B: Hepatitis B virus infection remains one of the major public health problems in the United States. Approximately 300,000 infections occur annually, causing 75,000 cases of acute hepatitis, 25,000 cases of chronic hepatitis, and 5,000–6,000 deaths from these diseases, cirrhosis, and liver cancer. The cost of this disease exceeds $720 million per year. Disease occurs primarily in young adults at risk because of lifestyle or occupation, but about 30 percent of cases occur in persons not belonging to any defined risk group. An effective hepatitis B vaccine became available in 1982, and immunization was recommended for groups at high risk of infection. Despite immunization of more than 1.4 million persons, disease incidence has increased by 50 percent in recent years. The primary reason for this failure of current immunization programs has been the difficulty in delivering vaccine to adult high-risk groups. The high cost of vaccine has also been a major constraint. This failure has necessitated the development of a new vaccination strategy. There are several parts to this new strategy, each to be implemented in sequence: first, universal screening of pregnant women and immunization of infants born to hepatitis B virus-carrier mothers; at the same time, continuation of immunization of individuals in high-risk groups (e.g., health-care workers, refugees from endemic-disease areas, persons using STD clinics, drug users accessed through rehabilitation programs or prisons); at the same time, continuation of immunization programs in areas of high endemicity of infection; later, universal immunization of infants; and finally, universal immunization of adolescents. This is an ambitious long-term program, worthy of the mission of the Centers for Disease Control. This approach could eliminate hepatitis B transmission as a significant health problem by the year 2015. This strategy would lead to prevention of disease by providing immunity from infection prior to initiation of risk-taking behavior in adolescence and young adulthood and would eliminate the 30 percent of infections in persons without known risk factors. This strategy will be most effectively accomplished by utilizing the established health-care system, at the point of prenatal care, birth in the hospital, routine infant immunization, and various school or special health encounters.

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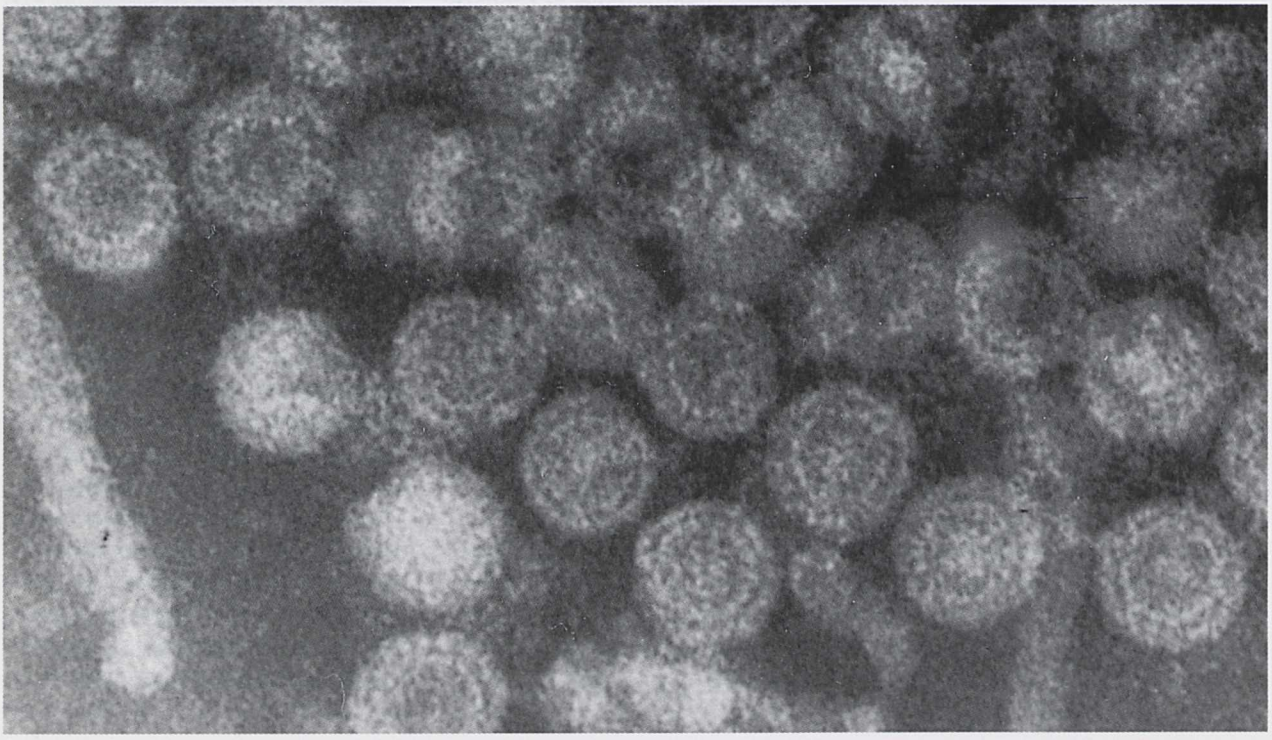
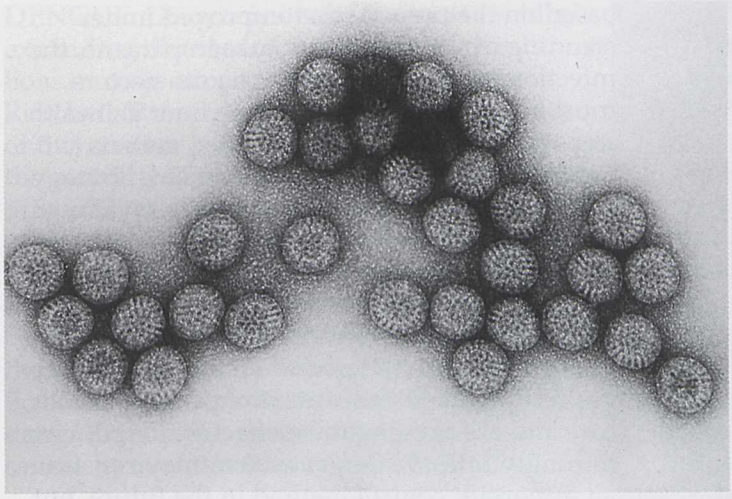




in the Center for Infectious Diseases, work on rotavirus diarrhea includes laboratory analysis of viral genetic and antigenic diversity and assessment of candidate vaccines—the goal is a vaccine for all children

ROTAVIRUS DIARRHEA: Rotavirus is the most common cause of serious diarrhea in American children. Every child is infected in its first three to four years of life, leading to an estimated three million cases of diarrhea, 500,000 doctor visits, 70,000 hospitalizations for 300,000 inpatient days, 75–125 deaths, and costs of hospital care of $200–400 million per year. Worldwide, nearly one million children die each year of rotavirus diarrhea. Vaccines currently being developed are likely to provide a means to prevent this important cause of childhood mortality and morbidity. In the Center for Infectious Diseases, field studies are addressing basic questions about safety and efficacy of different candidate vaccines. Information from these studies, plus laboratory-based studies on the genetic, antigenic, and immunologic characteristics of rotaviruses, should pave the way for identifying a safe and effective vaccine that can be incorporated into routine childhood immunizations. Through a national surveillance and laboratory program, patterns of virus transmission and virus variation are being determined. This information, coupled with mortality and hospitalization data, provides estimates on the disease burden and will allow monitoring of rotavirus vaccination programs in the future.

GIARDIASIS: Enteric parasitic diseases are being recognized with increasing frequency in the United States; an estimated four million people are affected by *Giardia lamblia* every year. Costs for diagnostic tests, therapy, hospitalization, and absence from work are estimated to be more than $120 million per year. The number of waterborne outbreaks of giardiasis has increased significantly in recent years; the organism has been implicated in 37 percent of 378 waterborne outbreaks of diarrhea investigated since 1976. Waterborne transmission most often occurs because of ineffective filtration or inadequate pretreatment of surface water (lakes, rivers, and streams) by municipal utilities. *Giardia* is also a well-recognized cause of diarrhea outbreaks in day-care centers and is also an endemic pathogen in day-care centers. In outbreak investigations, 10–50 percent of diaper-aged children have been found to be infected, and *Giardia* has been identified in 10–15 percent of diaper-aged children attending day-care centers. Spread of the organism in day-care centers is favored by close interpersonal contact, frequent hand-to-mouth and object-to-mouth behavior, and fecal incontinence. While secondary spread of *Giardia* is especially frequent among toddlers, transmission to children of other ages, child-care workers, and household

efforts to reduce transmission of **Giardia** *include identification of risk factors, development and assessment of control strategies, and application of better diagnostic techniques*

contacts is also common. About 20–25 percent of day-care center staff and family contacts of infected children become infected. The goal of the program of the Center for Infectious Diseases is to reduce transmission of *Giardia* through identification of risk factors, development and implementation of control strategies that address these risk factors, evaluation of the efficacy of control strategies, and development of more rapid and sensitive diagnostic techniques.

MALARIA: Malaria is one of the most prevalent and important infectious diseases in the world; it is estimated that 200–400 million persons are infected or reinfected annually. The highest mortality is in young children and pregnant women. In Africa, south of the Sahara, the most virulent malarial species, *Plasmodium falciparum*, is the cause of 5 to 12 percent of all deaths. In the United States, malaria is transmitted occasionally in California and in southeastern states, but more importantly, every year several million people are exposed in the course of international travel, and approximately 1,000 cases are reported in returning travelers. The spread of *Plasmodium falciparum* strains resistant to malaria drugs, especially chloroquine, complicates prevention recommendations for travelers. The program of the Center for Infectious Diseases is focused on increasing the proportion of travelers using effective prevention methods; improving surveillance of infected travelers returning to the United States; developing strategies for the control of malaria-associated mortality in Africa, via collaboration with concerned national governments and the World Health Organization; and defining the clinical and immunologic bases for naturally acquired immunity to malaria. These epidemiologic and laboratory approaches are based on the premise that improved understanding of the malaria protozoan parasite, the infection it causes, and its mosquito vectors must be at the heart of efforts to limit its health impact. In the tropics, historically, malaria control has relied on insecticides. This strategy, while highly effective in some areas, is failing in many other areas because of the high cost and potential toxicity of insecticides. In this situation, more effort is being devoted to community-based programs to assure prompt and effective therapy for acutely infected children; these programs operate in the context of primary health care and are proving to be effective in reducing mortality rates. Malaria vaccines may constitute an important control method in the future, but for the present, expansion of therapy programs is the most realistic and affordable approach available.

malaria is one of the most important infectious diseases in the world—it is estimated that 200–400 million persons are infected annually—in sub-Saharan Africa malaria is the cause of 5–12 percent of all deaths—highest mortality is in young children and pregnant women

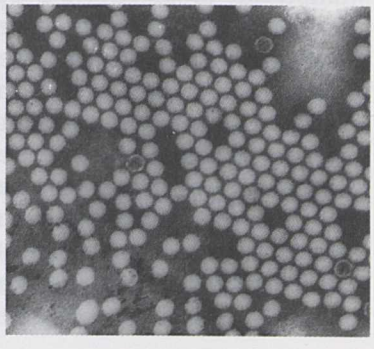
DENGUE: Dengue is one of the most rapidly expanding diseases of the tropics, with millions of cases occurring each year. Puerto Rico had five epidemics in the first 75 years of this century but has had six epidemics in the past 11 years, at an estimated cost of over $150 million. Dengue transmission has occurred twice in the continental United States in the past few years after an absence of thirty-five years. At the same time, there has been a record number of cases elsewhere in the Americas; Brazil, Bolivia, Paraguay, and Ecuador have experienced their first major dengue epidemics in over fifty years. The severe form of the disease, dengue hemorrhagic fever, is a leading cause of hospitalization and death of children in southeast Asia; in 1987 there were over 600,000 cases reported. Dengue hemorrhagic fever first occurred in the Americas in 1981, in association with a major epidemic in Cuba. Since then, eleven countries in the Western Hemisphere have reported cases of dengue hemorrhagic fever, suggesting that this manifestation of dengue infection is evolving in the Americas now as it did in southeast Asia in the 1960s. In the absence of effective continuous mosquito control, again because of the high cost and concern over potential toxicity of insecticides, early warning of the presence of virus is the key to predicting impending epidemics. If epidemics can be predicted, they can be prevented by focused mosquito control. The Center for Infectious Diseases coordinates an international surveillance system for the Americas in cooperation with the Pan American Health Organization and national health ministries; this includes laboratory-based reference diagnostics and field-based serologic and mosquito vector surveillance in dengue-endemic countries.

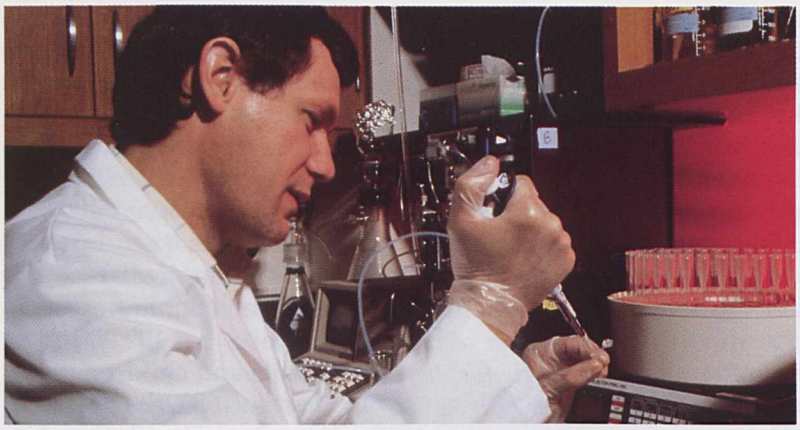
Aedes albopictus, *a newcomer to the Western Hemisphere and a proven vector of dengue virus*

a poster used in Puerto Rico as part of a public education program run by the Center for Infectious Diseases and Commonwealth and local health departments

POLIOMYELITIS: Paralytic poliomyelitis remains a serious public health problem in the developing countries of Africa and Asia—it still strikes as many as 400,000 children per year. In some endemic-disease areas, attack rates exceed 250 cases per 100,000 infants and children per year. In 1985, the Pan American Health Organization proposed the elimination of poliomyelitis from the Americas by the year 1990. To mobilize the substantial laboratory support required for this program, the Center for Infectious Diseases has led the development of a network of collaborating laboratories throughout the Americas, pioneered in developing improved methods for identifying wild polioviruses, transferred these methods within the network, and provided training and direct laboratory support to network laboratories. This effort, and the national polio vaccination programs carried out in all countries of the Americas, has been a great success. Now, the World Health Organization proposes total eradication of polioviruses from the world by the year 2000. This will require even more precise, rapid, and sensitive methods for the identification of wild polioviruses in much more difficult circumstances. Virologic data will have to be provided to indicate problem areas in national immunization programs so that vaccination resources can be directed most effectively.

poliovirus type 1 , electron micrograph , magnification x180,000



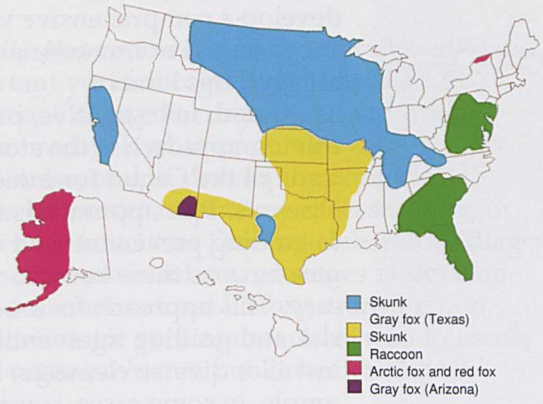


papillomaviruses, which are associated with cervical and esophageal cancer, cannot be grown in the laboratory—recombinant-DNA technologies are used in the Center for Infectious Diseases for detecting and typing these viruses in clinical specimens

PAPILLOMATOSIS AND CANCERS OF THE CERVIX AND ESOPHAGUS: The association between human papillomavirus infection and cancers is now firmly established. More than 85 percent of intraepithelial and invasive cervical cancers contain papillomavirus DNA. The same kind of association between papillomaviruses and esophageal cancer is suggested by the identification of viral DNA in tissues of 30–50 percent of cases. These findings do not explain how papillomaviruses cause these cancers, but they do focus attention on specific diagnostic approaches for early detection of infection, so as to guide clinical management and the prevention of transmission—and they point to a longer-term goal of prevention of these cancers by papillomavirus vaccination. This is a worthy enterprise: despite reductions in cervical cancer rates in the United States in recent years (because of cytologic screening programs and earlier surgical intervention), there are still 7,000 deaths per year, and there is a threat that this will increase because of dramatic increases in the incidence of genital papillomatosis. Papillomaviruses cannot be grown in cell cultures, so recombinant-DNA and synthetic peptide technologies are used in the Center for Infectious Diseases for diagnosis and further research: viral DNA amplification from small tissue biopsies (via the polymerase chain reaction—PCR) allows detection of the presence of virus and even allows identification of the viral type—there are more than 55 human papillomaviruses. A few of these viruses that have been best studied have distinct associations with particular types of precancerous lesions, and these lesions differ in their probability of progressing to cancer. In the Center for Infectious Diseases, efforts center on determining the risk associated with infection by the most recently discovered papillomavirus; this work involves analysis of unusual lesions and typical lesions in women in isolated populations with high incidences of disease, such as Alaskan Natives. This work will further our understanding of the genetic diversity of these viruses and will lead to better diagnostic tests and better prevention strategies.

RABIES: Rabies is still an important human disease in several areas of the world; for example, rabies kills some 50,000 people per year in India. Animal rabies is important in many more areas, including the United States, where diagnostic laboratory responsibilities are growing as wildlife rabies increases. Foxes, skunks, raccoons, and insectivorous bats maintain the virus in nature in various parts of the United States and transmit rabies to humans. Attempts to control wildlife rabies by poisoning or trapping animals have proved ineffective, so wildlife vaccination programs are emerging as the method of choice. Vaccines suitable for use in wildlife species are under development in the Center for Infectious Diseases: genes for the important antigens of rabies virus have been cloned and genetically transferred by recombinant-DNA technology into a harmless poxvirus (either vaccinia virus, which is the licensed smallpox vaccine virus, or raccoonpox virus, a nonpathogenic virus found in nature). The poxvirus serves as the carrier or vector of the rabies virus genes, but the vectored poxvirus cannot cause rabies. A similar approach involves the use of canine hepatitis virus as a vector; this virus is also found naturally in wild animals. When the vectored virus is inoculated, it grows to a limited extent, and while doing so it expresses the rabies antigens. These antigens evoke a protective immune response, so that if later the vaccine recipient is exposed to rabies virus, there is no infection or

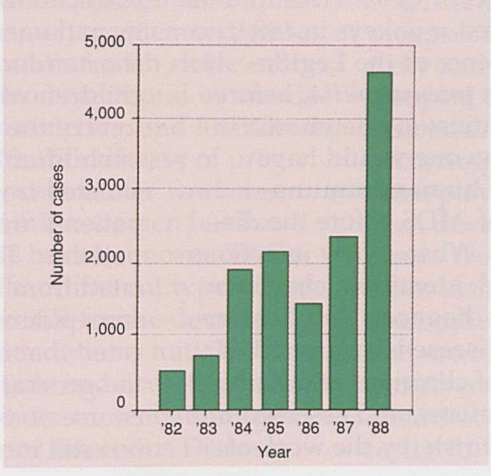
Distribution of 5 antigenic variants of rabies virus and the predominant wildlife species affected



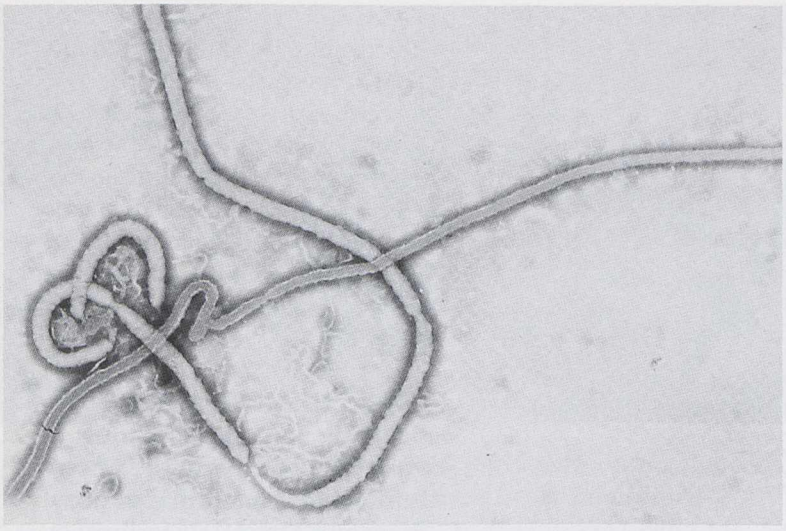
studies in the Center for Infectious Diseases, using monoclonal antibodies, have shown that different rabies virus strains are separately transmitted among different wild animal species—each must be dealt with specifically

disease. These vaccines have been tested in experimental animals in the laboratory and are now ready for comprehensive animal field trials. To protect wild animals, these vaccines will be delivered in baits that are attractive to particular species, such as raccoons and foxes. These vaccines offer for the first time an opportunity to control wildlife-borne rabies, and at the same time they offer an opportunity to protect dwindling wildlife resources.

LYME DISEASE: Since the first cases of Lyme disease were described in 1976, the disease has extended far beyond the originally recognized foci in the Northeast to involve most states. It is estimated that there are more than 10,000 cases occurring annually in the United States, more than the total of all other vector-borne diseases combined. Increased recognition and reporting are only partially responsible for this increase: convincing arguments have been advanced that the number and range of the principal tick vector, *Ixodes dammini*, have increased because of the increase in the population of white-tailed deer on which the tick feeds. Expanded surveillance and research projects are under way in the Center for Infectious Diseases; these include the evaluation of strategies to prevent exposure (using personal protective measures and ecologic modifications), field studies to define vectors in areas of the country outside the range of *Ixodes dammini*, and development and evaluation of new diagnostic tests.



VIRAL HEMORRHAGIC FEVERS: Some viruses must be worked with only in the Maximum Containment Laboratory (Biosafety Level 4): Marburg, Ebola, Lassa, Junin (the cause of Argentine hemorrhagic fever), Machupo (the cause of Bolivian hemorrhagic fever), Congo-Crimean hemorrhagic fever, and tick-borne encephalitis complex viruses. All of these viruses cause either severe hemorrhagic fever or severe encephalitis. There are no effective vaccines to protect laboratory workers against these viruses, so the integrity of the physical biocontainment facility and the reliability of staff operations are crucial for carrying out necessary diagnostic responsibilities and related applied research activities safely. All of these viruses cause important epidemic or sporadic diseases in the areas of the world where they occur; for example, it is estimated that there are more than 300,000 cases per year of Lassa fever in West Africa. The program of the Center for Infectious Diseases is focused on preventing the introduction of these viruses into the United States and on leading efforts to minimize the impact of these viruses in countries where they occur. These prevention and control programs are operated in cooperation with the World Health Organization and health ministries in the countries involved.



Ebola virus, electron micrograph, magnification x60,000 — in 1989-1990 a related virus was introduced into the United States in imported monkeys, prompting comprehensive quarantine actions

NEW AND EMERGING DISEASES, NEW AND EMERGING INFECTIOUS AGENTS, AND UNKNOWNS (DIAGNOSTIC SPECIMENS THOUGHT TO CONTAIN NEW PATHOGENS): New or previously unrecognized infectious agents are constantly being identified—the idea that "there is nothing new under the sun" is certainly not the case when it comes to infectious agents and infectious diseases. There is no way to predict when or where the next important new pathogenic microorganism will emerge. Likewise, there is no way to predict the significance of such a microorganism as it emerges—it might emerge as the cause of a geographically limited problem, or as the cause of new outbreaks, or as the cause of a new epidemic. No one would have predicted the emergence of **Marburg and Ebola viruses** from their still unknown econiches in Africa in 1967 and 1976, and no one would have predicted the introduction of Ebola virus into the United States via wild-caught imported monkeys in 1989; no one would have predicted the emergence of the **Legionnaires' disease bacterium, *Legionella pneumophila,*** before the investigation of the epidemic of unusual pneumonia in Pennsylvania in 1976; and certainly no one would have predicted the epidemic emergence of **human immunodeficiency virus, HIV**, as the cause of AIDS before the discovery of the virus in the early 1980s. When a new infectious agent is suspected, it must be isolated, identified, characterized, and developed into systems for diagnosis and field investigation. When a new infectious disease is suspected, it must be characterized (by the work of clinicians and pathologists and other clinical support specialists), and assessed in regard to its impact on populations at risk (by the work of medical epidemiologists and other support specialists). These activities must be highly integrated to develop a comprehensive view of the potential or immediate problem at hand; this kind of integrated, investigative, problem-solving approach is the stock-in-trade of the Center for Infectious Diseases. This approach is the key to guiding prevention and control measures as these become necessary. This approach for assessing risk and guiding intervention involves diverse elements; for example, in some cases, complex field studies of the incidence of infection in the general population or in selected subpopulations are necessary to determine risk factors for infection, mode of transmission, targets for intervention, etc., while in other cases, complex studies of pathogenetic mechanisms of the infection or the molecular biology of the agent hold the key to further action. The following examples illustrate this complex and diverse enterprise:

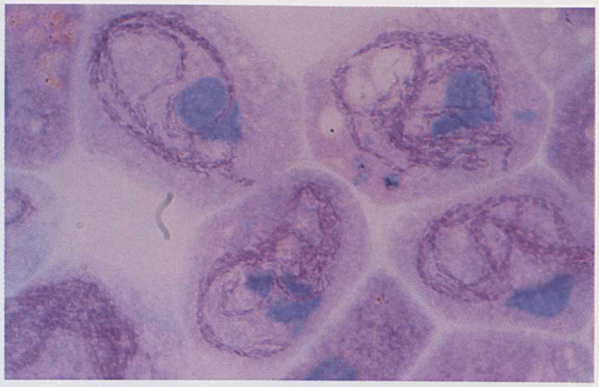
Human herpesvirus 6 was discovered just a few years ago; it was isolated first from an AIDS patient by a method that is used to isolate HIV, the causative agent of AIDS. Since then, the virus has been the subject of much investigation in the Center for Infectious Diseases. At first the virus was a curiosity, the subject of much speculation as to its pathogenic potential, but in short order it was isolated from children with roseola infantum (one of the common rash diseases of children), and then it was isolated from B-cell lymphoma patients and organ-transplant patients. The virus was also isolated from healthy adults, and seroepidemiologic studies indicated that infection is common in the general population. So, in the course of a few years a complex, but still incomplete, natural history

and public health picture has emerged from an initial misbelief that all human herpesviruses had already been discovered.

Chlamydia pneumoniae was discovered in 1986 as an important yet unrecognized cause of adult pneumonia. Chlamydial organisms had previously been recognized as important causes of genital disease, and in developing countries, blindness, but never respiratory disease. Now, in the Center for Infectious Diseases, laboratory diagnostic systems are in advanced stages of development, and further natural history, transmission, and epidemiologic studies are under way to assess this new organism's true public health impact.

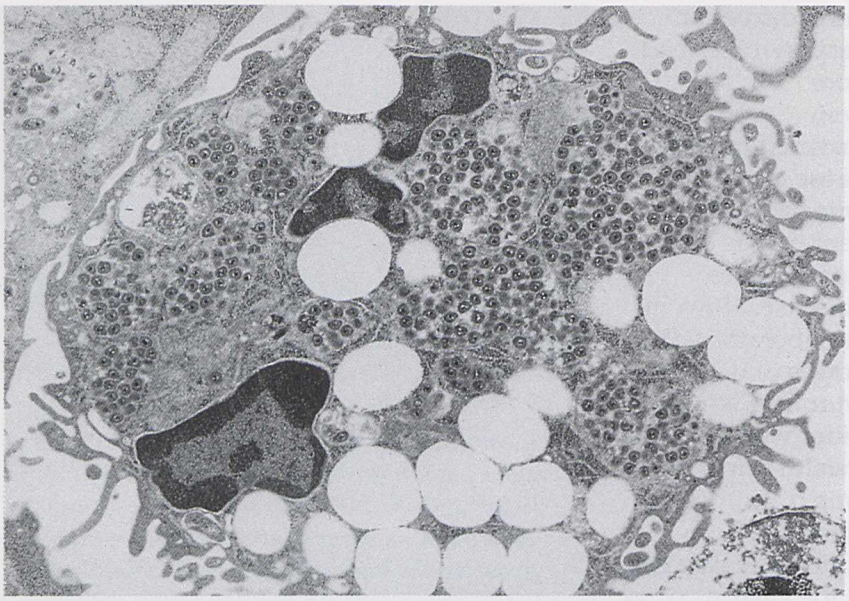
Helicobacter pylori was discovered in 1982 in association with gastritis and peptic ulcer disease. The bacterium has been found in the gastric mucosa of 75–90 percent of persons with chronic gastritis and 50–70 percent of persons with peptic ulcer disease, diseases that are often prolonged and painful, and require expensive medical and surgical therapy. The organism was also found in 20–40 percent of normal individuals. An unanswered question is whether the organism is the actual cause of gastritis or peptic ulcer disease or is just an incidental or opportunistic participant. If the organism proves to be a specific cause of these diseases, then simple, inexpensive treatment regimens (antimicrobial drug therapy) can be developed. Investigations to answer these outstanding questions are under way in the Center for Infectious Diseases.

Human parvovirus B19 was discovered a few years ago in England. Since then it has been shown to be the primary cause of erythema infectiosum (also called fifth disease, another of the common rash diseases of children) and aplastic crisis (an important hemolytic anemia disease, especially serious in association with sickle cell disease). The virus has also been found in association with arthritis, chronic anemia, and fetal death. Exposure by children with fifth disease of pregnant school teachers, day-care center workers, health-care workers, and other women has become an important public health concern. Defining the risk to the fetus after different types of maternal exposure is essential for the development of national recommendations; initial recommendations have been made and investigations necessary to extend these recommendations are under way in the Center for Infectious Diseases.



Legionella pneumophila, *the bacterium that causes Legionnaires' disease, has been found to grow intracellularly within free-living protozoa in some water supplies—this protects the bacterium from chlorination*

MODERN DIAGNOSTICS: Traditionally, diagnosis of infectious agents has depended on microscopic examination of clinical specimens or growth of the causative microorganism on an artificial medium or in cultured cells or in laboratory animals. While such methods may still be most appropriate in some cases, in too many other cases diagnosis has failed because of insensitivity of the method, intractable characteristics of the organism, or inactivation of the sample in transport. Two major research developments have occurred in recent years that open new prospects for diagnosis, namely the development of monoclonal antibodies and the development of recombinant-DNA (genetic engineering) technologies. Both offer the prospect for major improvements in the specificity and consistency of diagnostic reagents. Coupled with advances in the electronics of instrumentation, breakthroughs are constantly occurring; the Centers for Disease Control often plays a role as a leader or partner in such developments. Techniques being applied across the wide spectrum of infectious diseases include: (a) development of **monoclonal antibodies** specific for the various antigens that are common to groups of microorganisms (for screening tests) or limited to specific strains of microorganisms (for identification tests); (b) development of **immunologic test**



human herpesvirus 6, electron micrograph of an infected cell—in 1986 the virus was isolated first from an AIDS patient, next from children with roseola infantum (one of the common rash diseases of children), and then from B-cell lymphoma patients and organ-transplant patients

formats suitable for automated instruments (for large scale seroepidemiologic studies and intervention programs); (c) development of **synthetic peptides** and genetically engineered proteins suitable as antigens in diagnostic tests; (d) development of **synthetic and genetically engineered microbial nucleic acids for use as probes** in assays to detect infectious agents in tissues and other diagnostic specimens; and (e) development of **microbial gene amplification technologies** to detect exceptionally low levels of DNA or RNA of infectious agents (e.g., polymerase chain reaction—PCR, and Q-beta replicase reaction—QBR technologies). For example, gene amplification technology is being used for the early diagnosis of Rocky Mountain spotted fever. This technology will permit earlier use of antimicrobial drug therapy. In a similar way, the polymerase chain reaction and monoclonal antibody-based dot-blot immunoassays are being used to identify *Listeria monocytogenes* in contaminated food products. These methods take 18 hours rather than the 3–4 days of traditional methods, thereby accelerating appropriate public health actions to remove contaminated food products from markets. As another example, a Western blot assay has been developed for neurocysticercosis, a central nervous system disease caused by a tapeworm. This disease is increasing in the United States, especially in new immigrants from South America. The disease is confusing to physicians, who must differentiate it from brain tumors by CAT scan or other imaging techniques. The innovative laboratory assay developed in the Center for Infectious Diseases obviates unnecessary surgical procedures because the tapeworm may be eliminated with medication.

MODERN VACCINE DEVELOPMENT AND APPLICATION: Whoever coined the old saying, "an ounce of prevention is worth a pound of cure," may have had vaccines against infectious diseases in mind. Treatment of infected people is not always successful and can be difficult, expensive, and very demanding of the time of medical personnel. Prevention of disease by use of vaccines, on the other hand, is usually simple, safe, inexpensive, and long-lasting in effect. In some cases, vaccine use even offers the possibility for disease eradication, as has been the case with smallpox. Most present vaccines are composed either of inactivated or living-attenuated microorganisms; these vaccines have many positive attributes, but there are often shortcomings as well. Advances in biotechnology are providing unique opportunities for the development of entirely new types of vaccines. In the Center for Infectious Diseases, research and development activities are being carried out in collaboration with other agencies and institutions: important pathogenic microorganisms are being "taken apart," and their proteins (antigens) are analyzed to determine which are the best stimulators of protective immunity; genes coding for these antigens are then cloned (selectively amplified) using recombinant-DNA technology, and the genes are expressed to produce large amounts of antigens that can be formulated into vaccines. One such program in the Center for Infectious Diseases concerns malaria vaccine development.

prevention of disease by use of vaccines is usually simple, safe, inexpensive, and long-lasting in effect

Malaria parasites cannot be grown in culture in the laboratory, so traditional methods of developing vaccines have not been feasible. However, in the past few years in three institutions around the world, the genes for the important proteins of malaria parasites have been cloned, their DNA sequences determined, and from this information the amino acid sequences of their proteins have been predicted. These amino acid sequences have been used to chemically synthesize large amounts of proteins (peptides), which have been formulated into vaccines. In the Center for Infectious Diseases, these candidate vaccines are being injected into monkeys, which are then challenged with malaria parasites to evaluate their immunogenicity. Only by the use of such animal models can vaccines be judged ready for human trials—in this case, human trials are several years away, but there is a sense of hope that a new means of controlling malaria may be developed for use throughout tropical areas of the world. In the Center for Infectious Diseases, laboratory vaccine studies go hand in hand with epidemiologic studies; for example, studies of the incidence of diseases point out important target populations for new vaccine usage. Epidemiologic studies also allow evaluation of the efficacy, frequency of adverse reactions, and duration of immunity of new vaccines. For example, *Haemophilus influenzae* type b vaccine is one subject of combined epidemiologic and laboratory studies. This organism is the cause of serious disease, including meningitis, particularly in young children. Ongoing projects are evaluating the immune response in vaccinated children. These studies form an important part of the overall efforts in the United States to make available to all children effective vaccines against all important infectious diseases.

ANTIMICROBIAL DRUG RESISTANCE: Use of antimicrobial drugs in human and veterinary medicine and in animal feeds has resulted in the emergence of resistant bacterial pathogens. More recently, resistance has also emerged in fungal, parasitic, and viral agents, including HIV. In addition, medical advances in organ transplantation and the treatment of renal failure and cancer have introduced special problems in antibiotic usage. Antibiotic toxicity is an important cause of morbidity and may have significant economic and legal implications. Emergence of resistance provides challenges to improve surveillance of antimicrobial drug usage and resistance, apply modern laboratory techniques to determine mechanisms of resistance, and develop innovative strategies to ensure optimal antimicrobial drug usage to maximize clinical benefit and minimize emergence of resistant organisms in the future.

in the Center for Infectious Diseases important pathogenic microorganisms are being "taken apart" and their proteins assessed as stimulators of protective immunity—recombinant-DNA technology allows these proteins to be made in large amounts and formulated into candidate vaccines

WORLD HEALTH ORGANIZATION COLLABORATING CENTERS IN THE CENTER FOR INFECTIOUS DISEASES

WHO Collaborating Center for Reference and Research on Acquired Immunodeficiency Syndrome (AIDS)
WHO Collaborating Center for AIDS Research (Projet SIDA, Zaire)
WHO Collaborating Center for Reference and Research on Arboviruses
WHO Collaborating Center for Reference and Research on Dengue (pending)
WHO Collaborating Center for Reference and Research on Influenza
WHO Collaborating Center for Reference and Research on Respiratory Viruses Other Than Influenza
WHO Collaborating Center for Reference and Research on Viral Hepatitis
WHO Collaborating Center for Reference and Research on Rabies
WHO Collaborating Center for Reference and Research on Smallpox and Other Poxviruses
WHO Collaborating Center for Reference and Research on Enteroviruses
WHO Collaborating Center for Reference and Research on Viral Special Pathogens
WHO Collaborating Center for Reference and Research on Syphilis
WHO Collaborating Center for Reference and Research on *Escherichia*
WHO Collaborating Center for Reference and Research on *Klebsiella*
WHO Collaborating Center for Reference and Research on *Salmonella*
WHO Collaborating Center for Reference and Research on *Shigella*
WHO Collaborating Center for Reference and Research on Plague
WHO Collaborating Center for *Staphylococcus* Phage Typing
WHO Collaborating Center for Enteric Phage Typing
WHO Collaborating Center for Reference and Research on Rickettsia
FAO/WHO Collaborating Center for the Epidemiology of Leptospirosis
WHO Collaborating Center for Mycotic Diseases
WHO Collaborating Center for Host and Parasite Studies on Malaria
WHO Collaborating Center for Research, Training, and Control of Dracunculiasis
WHO Collaborating Center for Research on Basic Principles of Insecticide Formulations
WHO Collaborating Center for Human Immunoglobulins
WHO Collaborating Center for Reference and Research on Antibiotics and Antibiotic Substances
WHO Collaborating Center for Reference and Research Services for Standardization of Diagnostics

OTHER WORLD HEALTH ORGANIZATION COLLABORATING CENTERS
AT THE CENTERS FOR DISEASE CONTROL THAT RELATE TO THE PROGRAMS
OF THE CENTER FOR INFECTIOUS DISEASES:

WHO Collaborating Center for Applied Biosafety Programs and Training
WHO Collaborating Center for Classification of Diseases in North America
WHO Collaborating Center for Development of Integrated Primary Care Programs for Community Practice
WHO Collaborating Center for Research Training in Human Reproduction
WHO Collaborating Center for Immunization Activities
WHO Collaborating Center for Epidemiology Training
WHO Collaborating Center for Occupational Health
WHO Collaborating Center for Perinatal Care and Health Service Research in Maternal and Child Health
WHO Collaborating Center for Disaster Preparedness and Response

THE DIVISIONS AND PROGRAMS OF THE CENTER FOR INFECTIOUS DISEASES

DIVISION OF BACTERIAL AND MYCOTIC DISEASES: The Division of Bacterial and Mycotic Diseases operates at the forefront of the microbiologic and infectious disease sciences, fulfilling its mission of disease surveillance, epidemiologic and laboratory investigation, and reference services. The Division's activities encompass the many bacterial and mycotic diseases of public health importance in the United States and internationally. The Division's activities are advancing in scope and sophistication in keeping with ongoing changes in disease incidence and trends and in antimicrobial drug resistance patterns. The Division is in the midst of a technologic revolution, bringing more and more new and powerful approaches to bear on microbial and mycotic diagnostic and reference identification responsibilities. The Division is also in the midst of a revolution in epidemiologic and statistical approaches being brought to bear on important bacterial and mycotic diseases.

Even in this age of antimicrobial and antimycotic drugs, bacterial and mycotic agents continue to be the cause of many important enteric, respiratory, and central nervous system diseases. The nature of most bacterial and fungal diseases is such that a rapid response is the key to controlling episodes and outbreaks—epidemiologic investigation, special disease surveillance, laboratory studies, and consultation with concerned State and local health agencies must usually be done without delay—the Division takes pride in its reputation for rapid expert response.

The Division's laboratories support its epidemiologic activities by defining involved etiologic agents, developing diagnostic tests, studying how bacterial and mycotic agents cause illness, and serving as reference centers for State and other laboratories. The Division houses World Health Organization collaborating centers for several types of bacteria, including *Shigella, Salmonella, Escherichia, Leptospira,* and *Mycobacterium* , and also for mycotic agents of disease.

Societal and technologic changes are influencing the occurrence of bacterial and mycotic diseases. With advances in food processing and transport methods, opportunities for the development and spread of foodborne bacterial agents are increasing. New or previously little-known foodborne pathogens, such as *Escherichia coli* 0157:H7 and *Listeria monocytogenes,* call for revised surveillance approaches and prevention strategies. With the widespread use of antibiotics, new antimicrobial drug resistance patterns are becoming of great concern—this is especially the case with *Salmonella* species, *Shigella* species, *Streptococcus pneumoniae,* and *Staphylococcus aureus.* With the increase in numbers of immunocompromised patients (due to cancers, HIV infection, and the use of drugs in association with organ transplant surgery), there are new problems being caused by opportunistic mycotic and bacterial pathogens. Finally, societal changes have resulted in new infectious disease problems in new settings, such as in out-of-home child-care centers, hospitals, and extended-care facilities; increasing efforts are being made to deliver prevention and control strategies in such specialized settings. These and most other efforts require increasing cooperation between all concerned parties. In this regard, the Division is working hard to extend its collaborative efforts nationally and internationally with governmental, educational, and private agencies concerned with bacterial and mycotic disease prevention and control.

DIVISION OF HIV/AIDS: The Division of HIV/AIDS is actively involved in efforts to characterize human immunodeficiency virus (HIV) infection and to define the scope and magnitude of the acquired immunodeficiency syndrome (AIDS) epidemic in the United States and around the world. These efforts center

around HIV/AIDS surveillance activities and national and international epidemiologic and laboratory investigations.

In collaboration with State, local, and territorial health departments, the Division conducts and manages national surveillance of AIDS cases and coordinates studies of the incidence and prevalence of HIV infection in the United States. Begun in 1981, AIDS case surveillance has provided the scientific basis for HIV/AIDS prevention and control recommendations and continues to yield essential information about the epidemiologic features of this disease. As surveillance methods are expanded to include the full spectrum of HIV disease, these data will continue to be an essential element in the overall assessment of the impact of the HIV epidemic. Complementing AIDS case surveillance, HIV surveillance is conducted through the "family" of seroprevalence surveys, a national network of surveys and studies in selected subgroups across geographically diverse areas of the United States. The addition of these data to the body of knowledge about HIV/AIDS broadens our understanding of the dynamics of the epidemic substantially.

Taken together, AIDS surveillance data and HIV seroprevalence data provide information for monitoring the HIV/AIDS epidemic. These data allow the determination of infection trends in risk groups and trends in HIV transmission. In turn, these data allow AIDS case projections into the future, thereby supporting projections of national resource needs for future prevention and treatment programs.

Epidemiologic studies conducted in collaboration with health departments, medical centers, blood banks, and other national organizations and through collaborative agreements internationally have identified HIV risk factors and transmission patterns and clarified the natural history of HIV infection in adults and children. Ongoing studies will refine what is already known and provide further insight into areas such as biologic factors influencing HIV transmission, viral infectivity and virulence, and issues related to drug use. Laboratory investigations have resulted in the development of procedures for HIV isolation, characterization, and serodiagnosis. The Division's laboratories serve as a national reference center for HIV-1 and HIV-2 serologic testing. Important advances in our understanding of the nature of HIV infection have come through the the initial application of the polymerase chain reaction technique. HIV viral genome sequence analyses, improved Western blot methodology, and novel immunoassays have also contributed to our understanding of the natural history of HIV and to the pathogenesis of the disease AIDS.

The Division also provides epidemiologic, surveillance, and technical advice and assistance to State and local health departments, other governmental agencies, and medical institutions. The Division serves as a World Health Organization Collaborating Center for Reference and Research on HIV/AIDS.

DIVISION OF IMMUNOLOGIC, ONCOLOGIC, AND HEMATOLOGIC DISEASES: The Division of Immunologic, Oncologic, and Hematologic Diseases conducts integrated epidemiologic and laboratory investigations into the roles of infectious agents in cancer and diseases of the immune and hematologic systems, applying investigative and analytical epidemiologic methods and state-of-the-art molecular biologic techniques to important disease problems of today.

The Division works to clarify biologic processes involved in the development of certain diseases, and works to find the etiologic agents of certain diseases which on the basis of epidemiologic patterns and trends seem to be transmitted from person to person. In each case, preventive measures are sought. The Division is focusing its etiologic agent searching on Hodgkin's disease, leukemias, and lymphomas. Methods for early detection of tumors are being tested by epidemiologic field studies of certain leukemias and bladder cancers. The Division also conducts investigations to improve the sensitivity, specificity, accuracy, and efficiency of immunodiagnostic laboratory methods, and develops immunochemical methods and reagents for detecting and identifying infectious agents of public health importance. The Division also provides reference diagnostic tests in hematology, immunohematology, clinical chemistry, and hemoglobinopathies.

DIVISION OF PARASITIC DISEASES: The Division of Parasitic Diseases is concerned with the important protozoan and helminthic diseases of the United States and developing countries of the tropics. The Division is staffed by a multidisciplinary group of medical epidemiologists, parasitologists, immunologists, molecular biologists, analytical chemists, and entomologists involved in surveillance, epidemiologic investigations, and field and laboratory research. The Division collaborates closely with a wide spectrum of local, national, and international groups including State and local health departments, the Carter Presidential Center of Emory University, the World Health Organization, the United States Agency for International Development, and the United States Peace Corps.

Parasitic diseases represent significant health problems in the United States. Major domestic programs of the Division deal with malaria and other parasitic diseases in U.S. travelers to other countries, infectious diseases in out-of-home child-care centers, opportunistic infections in AIDS patients, and waterborne diseases.

The Division also has extensive international activities aimed at the prevention and control of malaria, filariasis, schistosomiasis, dracunculiasis (guinea worm disease), and intestinal parasites. The Division has field stations in Kenya and Guatemala involved in epidemiologic studies of these diseases.

The Division focuses its efforts in a variety of ways, including: 1) surveillance and epidemiologic investigation of parasitic diseases to define disease etiology, mode of transmission, and populations at risk and to develop effective methods for diagnosis, prevention, and control; 2) research and training in the epidemiology and control of arthropod vectors and intermediate hosts of human parasites; 3) epidemic aid and epidemiologic consultation; 4) reference diagnostic services for parasitic diseases to State health departments; 5) laboratory studies of parasitic infections, emphasizing in vivo and in vitro systems; 6) research, development, and evaluation of immunizing agents and the role of protective immunity in parasitic disease processes; and 7) scientific and technical assistance to various domestic and international groups.

DIVISION OF SEXUALLY TRANSMITTED DISEASES LABORATORY RESEARCH: The Division of Sexually Transmitted Diseases Laboratory Research applies modern microbiologic and immunologic methods to study the pathogenesis, genetics, immunology, and laboratory identification of the bacterial and chlamydial agents of sexually transmitted diseases (STDs). The Division provides laboratory support for collaborative studies on the epidemiology and treatment of such STDs as gonorrhea, syphilis, chancroid, and chlamydial and mycoplasmal infections.

An important focus of the Division is to define the extent and nature of the increasing resistance of *Neisseria gonorrhoeae* isolates to antimicrobial drugs. The Division is also studying changes in gonococcal organisms within communities and is working to identify and characterize gonococcal components that may be useful as a candidate vaccine. Another activity concerns the improvement of laboratory methods for the diagnosis of gonorrhea and for the determination of gonococcal antimicrobial drug susceptibility.

In view of the growing number of chlamydial infections in the United States today, the Division is increasing its efforts to accurately estimate chlamydia prevalence, to identify populations at risk, and to diagnose *Chlamydia* infections by rapid and sensitive laboratory methods.

The Division also investigates laboratory aspects of syphilis and other treponemal infections; consultation and reference diagnostic services for syphilis are provided for State and local health departments. The Division serves as a WHO Collaborating Center for Reference and Research on Syphilis.

DIVISION OF VECTOR-BORNE INFECTIOUS DISEASES: The Division of Vector-Borne Infectious Diseases investigates national and international outbreaks of viral and bacterial diseases transmitted to humans by arthropods. The Division conducts laboratory and epidemiologic research to improve the diagnosis of and prevention strategies for yellow fever, dengue, dengue hemorrhagic fever, Japanese encephalitis, plague, tularemia, relapsing fever, Lyme disease, and other vector-borne diseases.

The Division serves as a World Health Organization and Pan American Health Organization Collaborating Center for Reference and Research on Dengue and Dengue Hemorrhagic Fever. The Division manages an international training center in Puerto Rico for teaching dengue prevention and control methods to public health officers from throughout the Western Hemisphere. Within the Division are two other World Health Organization Collaborating Centers for Reference and Research, one for arboviruses and the other for plague. The Division maintains ties with public health agencies, universities, and medical research institutions throughout the world, with particular emphasis placed on vector control. The Division manages a national surveillance system and a national reference laboratory for Lyme disease. This, in turn, contributes importantly to collaborative studies with State and local health agencies to identify risk factors and to establish strategies for the prevention of Lyme disease.

DIVISION OF VIRAL AND RICKETTSIAL DISEASES: The Division of Viral and Rickettsial Diseases carries out comprehensive programs to prevent morbidity and mortality caused by the many viral and rickettsial diseases of national and worldwide importance. The Division fully integrates modern laboratory and epidemiologic sciences for the accomplishment of its mission; disease surveillance and epidemiologic field investigations are integrated with microbiologic and molecular biologic laboratory technologies and many special reference diagnostic services. The Division is conducting major programs for the prevention and control of hepatitis, influenza, viral respiratory diseases, viral diarrheal diseases, rickettsial diseases, zoonotic diseases, and diseases caused by exotic and dangerous viral and rickettsial pathogens. The Division's activities in these areas are leading to the application of new and novel prevention strategies throughout the United States and worldwide. Approaches include the refining of surveillance systems for assessing disease incidence and impact, developing innovative diagnostic approaches to allow early diagnosis and identification of etiologic agents, and designing focused epidemiologic studies of disease trends, natural history, and transmission patterns. For example, preventive measures for influenza have been improved significantly as a result of advances in surveillance techniques that permit earlier detection of antigenic variants and by the use of highly sensitive tests for the rapid diagnosis and analysis of influenza viruses. The application of this kind of integrated disease prevention and control approach in turn leads to improved public health intervention strategies. For example, current national efforts to reduce the incidence of hepatitis B through universal immunization of infants and adolescents are based on continuing epidemiologic studies of disease trends and vaccine efficacy. The same kind of integrated disease prevention and control approach is being used to address new and emerging infectious diseases and to incriminate viruses as the cause of certain cancers and degenerative conditions. For example, hepatitis B has been shown to cause primary hepatocellular carcinoma, the most common cancer in the world, and associations have also been demonstrated for human papillomavirus and cervical cancer, Epstein-Barr virus and nasopharyngeal cancer, and HTLV-I and adult T-cell lymphoma. Within the Division, there are eight WHO Collaborating Centers for Reference and Research.

ARCTIC INVESTIGATIONS PROGRAM: The Arctic Investigations Program, located in Anchorage, Alaska, conducts epidemiologic and laboratory investigations on infectious disease problems of Arctic and sub-Arctic populations, especially Alaskan Natives (Eskimos, Aleuts, Indians). Program emphasis is on applied epidemiology; the latest knowledge and technology is used to direct programs for the prevention and control of diseases in widely scattered, sparsely distributed populations. Activities include disease surveillance, investigation of disease etiology, analytic and descriptive epidemiologic studies, development of laboratory methods, evaluation of intervention strategies, dissemination of information, and training in research, epidemiology, and public health.

Major emphasis is on prevention and control of hepatitis B, *Haemophilus influenzae* type b infection, and streptococcal pneumonia. Hepatitis B studies include evaluating long-term sequelae (cancer, cirrhosis) of infection, and detecting early resectable liver cancers through alpha-fetoprotein screening of carriers. In *Haemophilus influenzae* studies, the focus is on

immunogenicity studies of vaccines for infants under 6 months of age. In pneumococcal disease studies, increased surveillance, studies of disease incidence, characterization of isolates including serotype and antibiotic resistance, development of rapid diagnostic tests, and evaluation and better use of current pneumococcal vaccines are in progress.

Botulism and *Echinococcus multilocularis* infections are two diseases with unique impact in the Arctic. Botulism occurs after consumption of certain native foods. Studies are under way to assess the pharmacodynamics of antitoxin and to develop rapid laboratory methods for identification of toxin in food or body fluids. *Echinococcus multilocularis* infection results in severe liver disease; transmission to humans occurs by exposure to dogs or foxes. Control is focused on reducing primary infection and on screening the high-risk population with a newly developed blood test. Work is also ongoing on long-term sequelae of infectious diseases, particularly virus-associated cancers (such as cervical cancer, which is associated with papillomavirus infection). Much of this work is done via collaborative efforts involving the Indian Health Service, the State health department of Alaska, universities, and other agencies.

HOSPITAL INFECTIONS PROGRAM: The Hospital Infections Program conducts active surveillance and ongoing epidemiologic and laboratory investigations of existing as well as emerging nosocomial infection problems. These activities are designed to lower rates of and identify risk factors for hospital-acquired infections. The Program serves as a national focus for issuing recommendations and guidelines for prevention and control of hospital infections, including occupational HIV infections, and for sterilization and disinfection techniques for health-care settings.

The Program's National Nosocomial Infections Surveillance (NNIS) system provides national nosocomial infection rates to acute-care facilities, national health organizations, and the public. Since introduction of NNIS surveillance components in 1986, implementation has steadily increased. Knowledge of nosocomial infection rates can serve as a stimulus for facilities to evaluate their infection control programs and can provide a "benchmark" for national comparisons. Preliminary evidence has indicated that reporting these infection rates back to participating hospitals can result in significant reductions in nosocomial infections.

New laboratory research techniques, such as polymerase chain reaction and ribotyping, which allow for rapid detection and/or genetic characterization of nosocomial pathogens have recently been employed to study transmission of hospital infections. Molecular techniques are also being used to determine the mechanisms of bacterial resistance. The Program's laboratories serve as World Health Organization Collaborating Centers for *Staphylococcus* Phage Typing, for Reference and Research on *Klebsiella*, and for Antibiotics and Antimicrobial Substances.

The Program collaborates with national and international agencies and infection control organizations to reduce the incidence of nosocomial infections by evaluating current prevention strategies, such as those protecting health-care workers from acquiring bloodborne diseases from patients, as to their effect on the incidence of nosocomial infections in patients. Other priorities include the development of ways to improve the compliance of acute-care facilities with existing recommendations and guidelines. NNIS will continue to play a vital role in these programs by providing data to evaluate their efficacy.

SCIENTIFIC RESOURCES PROGRAM: The Scientific Resources Program procures, manages, and distributes the resources required by CDC investigators for research and service activities in laboratories and in the field. These resources are diverse in nature and demanding in scale and timeliness.

Laboratory animal facilities are fully accredited by the American Association for Accreditation of Laboratory Animal Care and operated under the supervision of veterinarians board-certified by the American College of Laboratory Animal Medicine. The Program conducts protocol reviews for research and diagnostic activities involving laboratory animals.

Cell cultures, cell culture media, and microbiologic media are produced using modern

methods and exhaustive quality assurance testing. The program also maintains an active applied research program in cell biology, and conducts research leading to the development of new cell culture systems and cell lines.

The Program procures, prepares, and distributes sterile glassware and plasticware, and provides packing, shipping, and receiving services for etiologic agents, diagnostic specimens, and reagents from the CDC catalog. The Program provides services for maintaining and developing laboratory equipment.

The Program houses the Center's Biotechnology Core Facility, providing instrumentation and expertise in DNA and protein/peptide synthesis and analysis.

STANDING COMMITTEES AND INTEREST GROUPS OF THE CENTER FOR INFECTIOUS DISEASES

The Center for Infectious Diseases Equal Employment Opportunity / Affirmative Action Advisory Committee

The staff of the Center for Infectious Diseases is committed to the principles of equal employment opportunity and affirmative action (EEO/AA) and supports the CDC Affirmative Employment Plan. As a part of this effort, the Center has established, as a permanent management resource, an EEO/AA Advisory Committee. The committee works to achieve racial, ethnic, and gender parity in all job categories.

The Center for Infectious Diseases Health and Safety Committee and Division and Program Health and Safety Committees

The Center for Infectious Diseases Surveillance Committee

The Center for Infectious Diseases / National Research Council Postdoctoral Fellowship Review Committee

The Center for Infectious Diseases Education Committee

The Center for Infectious Diseases Grand Rounds Committee

The Center for Infectious Diseases Information Resources Management Committee

The Centers for Disease Control / Center for Infectious Diseases Child-Care Health Task Force

The Center for Infectious Diseases Opportunistic Infections Working Group

The Center for Infectious Diseases Foodborne and Waterborne Diseases Working Group

The Center for Infectious Diseases Year 2000 Objectives Committee

The Center for Infectious Diseases Biotechnology Core Facility Advisory Committee

The Center for Infectious Diseases Animal Use Committee

The Center for Infectious Diseases Awards Committee

The Center for Infectious Diseases Project Proposal Review Committee

The Center for Infectious Diseases Molecular Biology Interest Group

The Center for Infectious Diseases Modern Diagnostics Interest Group

The Center for Infectious Diseases Statistics Interest Group

ORGANIZATIONAL MATTERS

Detailed information on the organizational structure of the Center for Infectious Diseases and a listing of Division and Program Directors and Branch Chiefs are available separately.

Partnerships between the Center for Infectious Diseases and its Constituencies

In carrying out their mission, the Divisions and Programs of the Center for Infectious Diseases work with many government, academic, and medical institutions to which they provide various research, clinical, and consultative services. The following are some of the Center's constituencies:

- Federal Agencies
  - National Institutes of Health
  - Indian Health Service
  - Food and Drug Administration
  - Department of Agriculture
  - Environmental Protection Agency
- State Health Departments
  - Association of State and Territorial Health Officials
  - Conference of State and Territorial Epidemiologists
  - Association of State and Territorial Public Health Laboratory Directors
- Local Health Departments
  - National Association of County Health Officials
  - United States Conference of Local Health Officers
- Medical and Biomedical Science Institutions
- Schools of Public Health
- World Health Organization, including Regional Offices

The Center for Infectious Diseases Board of Scientific Counselors

The Center for Infectious Diseases Board of Scientific Counselors was formed to involve leaders in the microbiologic / infectious disease sciences and community leaders in the affairs of the Center. The Board provides advice and makes recommendations concerning the Center's programs, program priorities, program redirection, and program resources. The Board meets twice a year.

FOR FURTHER INFORMATION

Employment Opportunities in the Center for Infectious Diseases

Employment opportunities in the Center for Infectious Diseases are announced according to federal regulations in official registers, and also in journals and newsletters and in letters to potential applicants and supervisors of potential applicants. For further information, contact the CDC Personnel Management Office, the Office of the Director of the Center for Infectious Diseases, or the Office of the Director of any Division or Program of the Center.

The CDC Epidemic Intelligence Service (EIS) Program in the Center for Infectious Diseases

CDC EIS officers assigned to the Center for Infectious Diseases participate fully in the wide range of scientific and public health activities, including epidemiologic studies, disease surveillance, public health policy development, and epidemic investigations throughout the United States and overseas, particularly in Latin America, Africa, and Asia. In addition, EIS officers play a prominent role in disseminating and communicating scientific and public health information by publishing papers in scientific journals and giving presentations at national and international meetings. EIS officers receive personalized on-the-job training from epidemiologists, laboratory scientists, and statisticians, many of whom are internationally renowned experts in their fields; officers rapidly develop expertise in epidemiologic investigation and disease prevention and control methodologies, and assume substantial responsibility during epidemic investigations and in the conduct of research projects. EIS officers have played a prominent role in identifying and investigating some of the most important infectious disease problems of recent years,

such as Legionnaires' disease, toxic shock syndrome, HIV infection, and Lyme disease. Major initiatives for the 1990s, which will involve EIS officers, include the prevention and control of HIV infection, the surveillance of Lyme disease, the interruption of hepatitis B transmission in the United States, the assessment and prevention of opportunistic infections in HIV-infected persons, the development of programs to prevent diseases in child-care settings, the surveillance of antimicrobial resistance trends in the United States, the prevention and control of nosocomial infections, and the further development of national risk assessment programs for foodborne diseases. For further information, contact the CDC Epidemiology Program Office.

The Center for Infectious Diseases / National Research Council Postdoctoral Fellowship Program

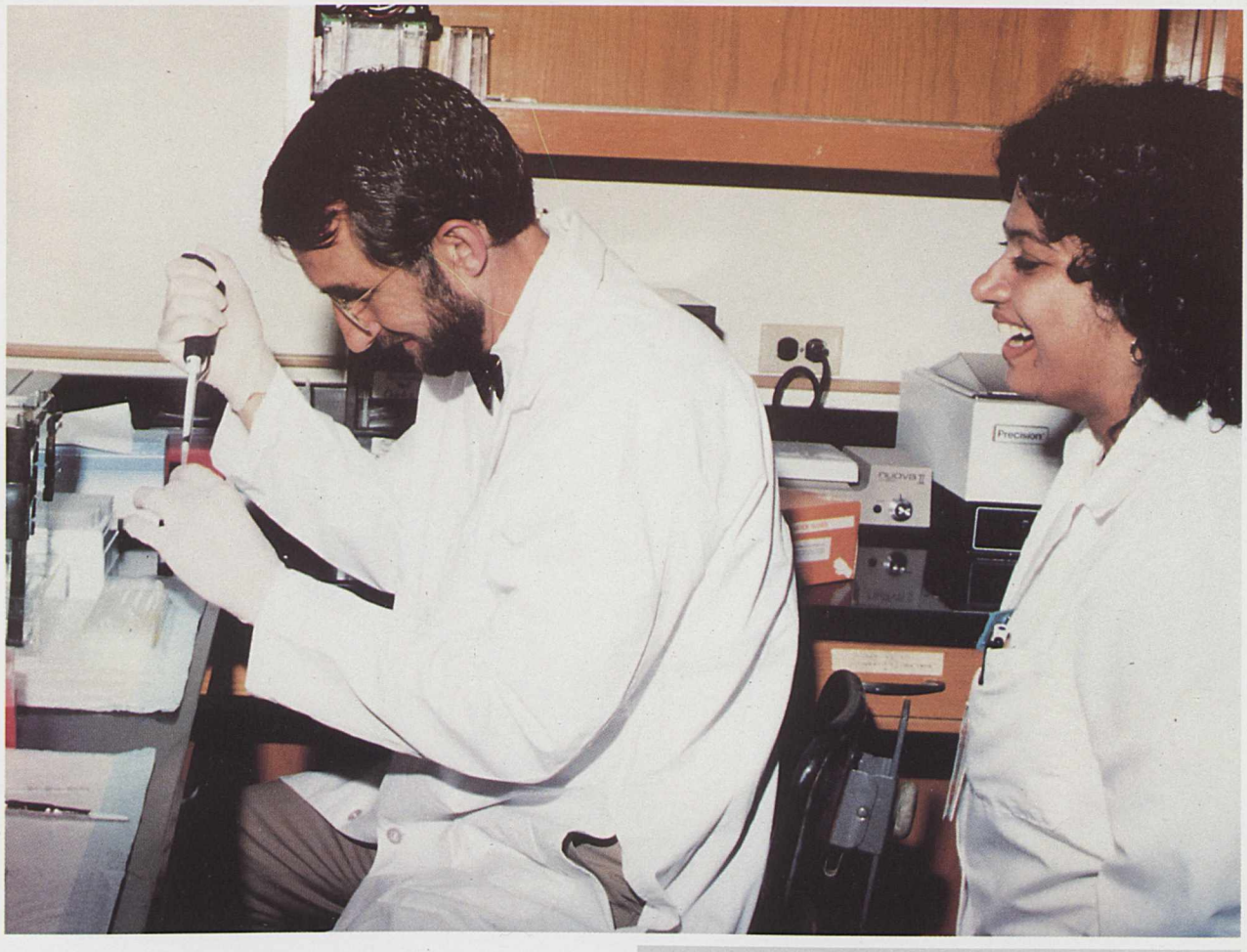
Since 1981, the Center for Infectious Diseases has been offering Resident Research Associateships (Postdoctoral Fellowships and Senior Fellowships) under the auspices of the National Research Council. These associateships are awarded competitively and provide recipients an opportunity for a concentrated research experience under the mentorship of selected staff scientists in each of the Divisions and Programs of the Center. In 1990, opportunities were available in 64 scientific areas, representing much of the disciplinary expertise of the Center, but emphasizing molecular biologic approaches in most instances. Candidates will find opportunities in areas as diverse as the use of poliovirus sequencing to track the course of outbreaks and epidemics internationally (molecular epidemiology), the rapid detection of the agents of bacterial meningitis, the molecular characterization of *Borrelia burgdorferi*, the biochemistry of gonococcal virulence, the molecular basis for *Candida albicans* virulence, the molecular genetics of *Anopheles* mosquitoes, and the pathogenesis of simian immunodeficiency virus infection—a model for AIDS. For further information, contact the Associate Director for Laboratory Science, Center for Infectious Diseases.

The Center for Infectious Diseases / Tuskegee University College of Veterinary Medicine Summer Fellowship Program

The Center for Infectious Diseases/Tuskegee University College of Veterinary Medicine Summer Fellowship Program began in 1988; its purpose is to encourage veterinary medical students to consider careers in public service, public health, biomedical sciences, and laboratory and epidemiologic approaches to the control and prevention of infectious diseases. Students and mentors are matched according to specific interests and goals: there are opportunities for gaining experience in microbiologic and molecular biologic laboratories, in laboratory animal medicine, and in epidemiology. This program is run in conjunction with CDC's cooperative agreement with the Association of Minority Health Professions Schools.

The Center for Infectious Diseases / Morehouse University School of Medicine Summer Fellowship Program

The Center for Infectious Diseases/Morehouse University School of Medicine Summer Fellowship Program began in 1989; its purpose is to encourage medical students to consider careers in public service, public health, biomedical sciences, and laboratory and epidemiologic approaches to the control and prevention of infectious diseases. Students and mentors are matched according to specific interests and goals: there are opportunities for gaining experience in microbiologic and molecular biologic laboratories, and in epidemiology. This program is run in conjunction with CDC's cooperative agreement with the Association of Minority Health Professions Schools.



the Director and the staff of the Centers for Disease Control would be delighted to respond to inquiries about career opportunities in any of the public health/preventive medicine professions

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